Access DB# 87301

SEARCH REQUEST FORM

Scientific and Technical Information Center

Requester's Full Name: Dwayne C. Jones Examiner #: 71294 Date: 24FEB03
Art Unit: 1614 Phone Number 30 8-4634 Serial Number: 09/921,477
Mail Box and Bldg/Room Location: 2007, CM1 Results Format Preferred (circle): PAPER DISK E-MAIL
2007, CM1

If more than one search is submitted, please prioritize searches in order of need. MEJ

****

Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc, if known. Please attach a copy of the cover sheet, pertinent claims, and abstract.

Title of Invention: see attached sheet

Inventors (please provide full names): 11

Earliest Priority Filing Date: 08/01/2000

For Sequence Searches Only *Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.*

Please search claim 1
and cross them with a:

(1) method of lowering blood pressure and systemic lipid concentration

(2) method of reducing risk of arterial + heart disease

78.00
69.00

Point of Contact:
Barb O'Bryen
Technical Information Specialist
STIC CM1 6A05 308-4291

****

STAFF USE ONLY

Searcher: Barb
Searcher Phone #:
Searcher Location:
Date Searcher Picked Up:
Date Completed: 2-25-03
Searcher Prep & Review Time: 20
Clerical Prep Time:
Online Time: 45

Type of Search

NA Sequence (#)
AA Sequence (#)
Structure (#)
Bibliographic X
Litigation
Fulltext
Patent Family
Other

Vendors and cost where applicable

STN 364
Dialog
Questel/Orbit
Dr.Link
Lexis/Nexis
Sequence Systems
WWW/Internet
Other (specify)

PTO-1590 (8-01)

```
=> fil reg; d stat que l5; d stat que l8
FILE 'REGISTRY' ENTERED AT 11:57:08 ON 26 FEB 2003
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Property values tagged with IC are from the ZIC/VINITI data file
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STRUCTURE FILE UPDATES:   25 FEB 2003  HIGHEST RN 494824-56-5
DICTIONARY FILE UPDATES:  25 FEB 2003  HIGHEST RN 494824-56-5

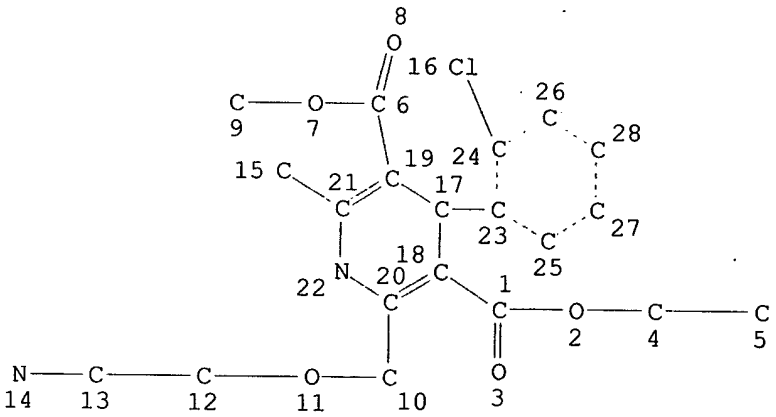
TSCA INFORMATION NOW CURRENT THROUGH MAY 20, 2002

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

Crossover limits have been increased.  See HELP CROSSOVER for details.

Experimental and calculated property data are now available.  See HELP
PROPERTIES for more information.  See STNote 27, Searching Properties
in the CAS Registry File, for complete details:
http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

L3                STR
```



amlodipine

family search done on this structure to retrieve salts, stereoisomers, isotopically labeled substances, & multi-component substances

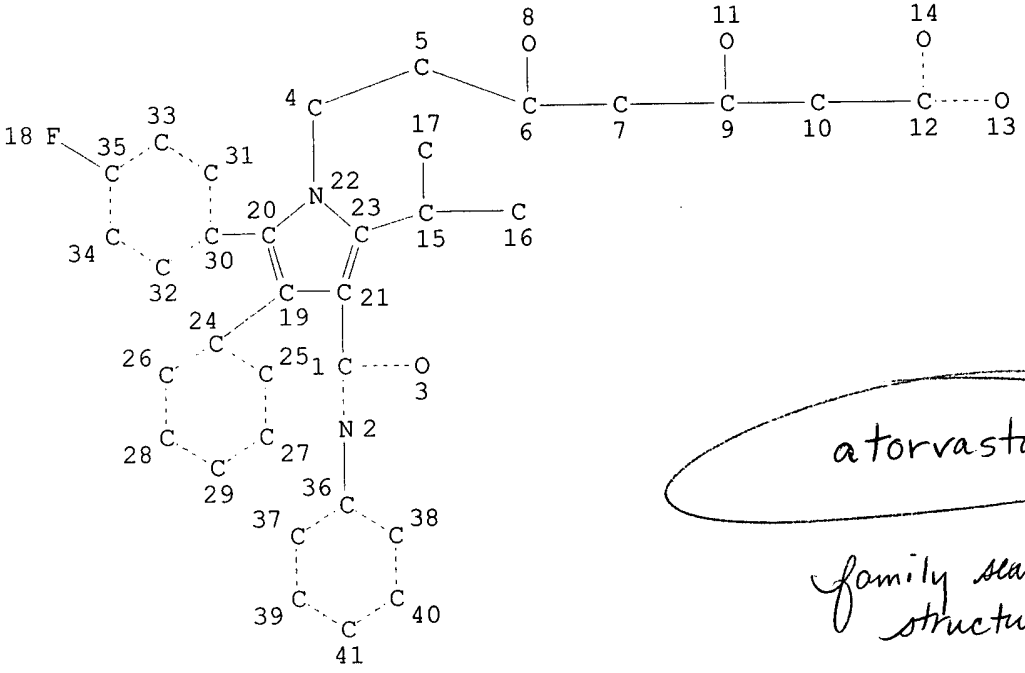
```
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS  28

STEREO ATTRIBUTES: NONE
L5            62 SEA FILE=REGISTRY FAM FUL L3

100.0% PROCESSED    373 ITERATIONS                    62 ANSWERS
SEARCH TIME: 00.00.01

L6                STR
```



atorvastatin

family search done on this structure

NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 41

STEREO ATTRIBUTES: NONE
L8 32 SEA FILE=REGISTRY FAM FUL L6

100.0% PROCESSED 51 ITERATIONS 32 ANSWERS
SEARCH TIME: 00.00.01

=> fil hcapl

FILE 'HCAPLUS' ENTERED AT 11:57:09 ON 26 FEB 2003
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FILE COVERS 1907 - 26 Feb 2003 VOL 138 ISS 9
FILE LAST UPDATED: 25 Feb 2003 (20030225/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> d que nos l31; d que nos l36; d que nos l38

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L3              STR
L5           62 SEA FILE=REGISTRY FAM FUL L3
L6              STR
L8           32 SEA FILE=REGISTRY FAM FUL L6
L11         760 SEA FILE=CAPLUS ABB=ON  L8
L24        1157 SEA FILE=HCAPLUS ABB=ON  L5 OR (AMLODIPIN? OR NORVASC OR
                PELMEC)/OBI
L25         815 SEA FILE=HCAPLUS ABB=ON  L11 OR (ATORVASTATIN? OR CI981 OR CI
                981 OR LIPITOR?)/OBI
L26       34267 SEA FILE=HCAPLUS ABB=ON  DRUG#(L)(INTERACT? OR SYNERG? OR
                POTENTIAT?)/OBI
L31           7 SEA FILE=HCAPLUS ABB=ON  L24 AND L25 AND L26


L3              STR
L5           62 SEA FILE=REGISTRY FAM FUL L3
L6              STR
L8           32 SEA FILE=REGISTRY FAM FUL L6
L11         760 SEA FILE=CAPLUS ABB=ON  L8
L24        1157 SEA FILE=HCAPLUS ABB=ON  L5 OR (AMLODIPIN? OR NORVASC OR
                PELMEC)/OBI
L25         815 SEA FILE=HCAPLUS ABB=ON  L11 OR (ATORVASTATIN? OR CI981 OR CI
                981 OR LIPITOR?)/OBI
L27       83247 SEA FILE=HCAPLUS ABB=ON  ?HYPERTENS?
L28       11065 SEA FILE=HCAPLUS ABB=ON  HYPOLIPEMIC?/OBI OR ANTICHOLESTEREMIC?
                /OBI
L29       43980 SEA FILE=HCAPLUS ABB=ON  ?ARTERIOSCLERO? OR ?ATHEROSCLERO?
L30      130274 SEA FILE=HCAPLUS ABB=ON  LIPIDS/CT
L33          21 SEA FILE=HCAPLUS ABB=ON  L24 AND L25 AND L27 AND (L28 OR L30)
L35          14 SEA FILE=HCAPLUS ABB=ON  L29 AND L24 AND L25
L36          12 SEA FILE=HCAPLUS ABB=ON  L33 AND L35


L3              STR
L5           62 SEA FILE=REGISTRY FAM FUL L3
L6              STR
L8           32 SEA FILE=REGISTRY FAM FUL L6
L11         760 SEA FILE=CAPLUS ABB=ON  L8
L24        1157 SEA FILE=HCAPLUS ABB=ON  L5 OR (AMLODIPIN? OR NORVASC OR
                PELMEC)/OBI
L25         815 SEA FILE=HCAPLUS ABB=ON  L11 OR (ATORVASTATIN? OR CI981 OR CI
                981 OR LIPITOR?)/OBI
L27       83247 SEA FILE=HCAPLUS ABB=ON  ?HYPERTENS?
L28       11065 SEA FILE=HCAPLUS ABB=ON  HYPOLIPEMIC?/OBI OR ANTICHOLESTEREMIC?
                /OBI
L29       43980 SEA FILE=HCAPLUS ABB=ON  ?ARTERIOSCLERO? OR ?ATHEROSCLERO?
L30      130274 SEA FILE=HCAPLUS ABB=ON  LIPIDS/CT
L33          21 SEA FILE=HCAPLUS ABB=ON  L24 AND L25 AND L27 AND (L28 OR L30)
L35          14 SEA FILE=HCAPLUS ABB=ON  L29 AND L24 AND L25
L37     1272999 SEA FILE=HCAPLUS ABB=ON  INTERACT? OR SYNERG? OR POTENTIAT?
L38           6 SEA FILE=HCAPLUS ABB=ON  (L33 OR L35) AND L37
```

=> s l31 or l36 or l38

```
L91          17 L31 OR L36 OR L38

=> fil medl; d que nos l43; d que nos l54

FILE 'MEDLINE' ENTERED AT 11:57:11 ON 26 FEB 2003

 FILE LAST UPDATED: 25 FEB 2003 (20030225/UP). FILE COVERS 1958 TO DATE.

 On June 9, 2002, MEDLINE was reloaded. See HELP RLOAD for details.

 MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the
 MeSH 2003 vocabulary. See http://www.nlm.nih.gov/mesh/summ2003.html
 for a description on changes.

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.


L3              STR
L5           62 SEA FILE=REGISTRY FAM FUL L3
L6              STR
L8           32 SEA FILE=REGISTRY FAM FUL L6
L40        1100 SEA FILE=MEDLINE ABB=ON  L5 OR AMLODIPINE/CT
L41         796 SEA FILE=MEDLINE ABB=ON  L8 OR ATORVASTATIN? OR CI981 OR CI
                981 OR LIPITOR
L42       91569 SEA FILE=MEDLINE ABB=ON  DRUG INTERACTIONS+NT/CT
L43           1 SEA FILE=MEDLINE ABB=ON  L40 AND L41 AND L42



L3              STR
L5           62 SEA FILE=REGISTRY FAM FUL L3
L6              STR
L8           32 SEA FILE=REGISTRY FAM FUL L6
L40        1100 SEA FILE=MEDLINE ABB=ON  L5 OR AMLODIPINE/CT
L41         796 SEA FILE=MEDLINE ABB=ON  L8 OR ATORVASTATIN? OR CI981 OR CI
                981 OR LIPITOR
L44      168691 SEA FILE=MEDLINE ABB=ON  BLOOD PRESSURE+NT/CT
L45       26282 SEA FILE=MEDLINE ABB=ON  ANTIHYPERTENSIVE AGENTS/CT
L46      156568 SEA FILE=MEDLINE ABB=ON  HYPERTENSION+NT/CT
L47        5612 SEA FILE=MEDLINE ABB=ON  ANTILIPEMIC AGENTS/CT
L48       34361 SEA FILE=MEDLINE ABB=ON  HYPERLIPIDEMIA+NT/CT
L49      116131 SEA FILE=MEDLINE ABB=ON  LIPIDS+NT/CT(L)BL/CT
L50       20575 SEA FILE=MEDLINE ABB=ON  LIPID METABOLISM, INBORN ERRORS+NT/CT

L51     1081583 SEA FILE=MEDLINE ABB=ON  CARDIOVASCULAR DISEASES+NT/CT
L54           1 SEA FILE=MEDLINE ABB=ON  L40 AND L41 AND (L44 OR L45 OR L46 OR
                L47 OR L48 OR L49 OR L50 OR L51)


=> s l43 or l54

L92           1 L43 OR L54

=> fil embase

FILE 'EMBASE' ENTERED AT 11:57:13 ON 26 FEB 2003
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 FILE COVERS 1974 TO 20 Feb 2003 (20030220/ED)

 EMBASE has been reloaded. Enter HELP RLOAD for details.
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This file contains CAS Registry Numbers for easy and accurate substance identification.

=> d que nos 165; d que nos 180; d que nos 181; d que nos 184

```
L55        4059 SEA FILE=EMBASE ABB=ON  AMLODIPINE/CT OR AMLODIPINE BESYLATE/CT

L56           1 SEA FILE=EMBASE ABB=ON  AMLODIPINE DERIVATIVE/CT
L57           5 SEA FILE=EMBASE ABB=ON  AMLODIPINE MALEATE/CT
L59        2021 SEA FILE=EMBASE ABB=ON  ATORVASTATIN/CT OR ATORVASTATIN
               LACTONE/CT OR ATORVASTATIN METHYL ESTER/CT
L60           1 SEA FILE=EMBASE ABB=ON  ATORVASTATINE/CT
L65           3 SEA FILE=EMBASE ABB=ON  ((L55 OR L56 OR L57))(L)CB/CT AND
               ((L59 OR L60))(L)CB/CT
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subheading CB = drug combination

```
L3               STR
L5            62 SEA FILE=REGISTRY FAM FUL L3
L6               STR
L8            32 SEA FILE=REGISTRY FAM FUL L6
L55        4059 SEA FILE=EMBASE ABB=ON  AMLODIPINE/CT OR AMLODIPINE BESYLATE/CT

L56           1 SEA FILE=EMBASE ABB=ON  AMLODIPINE DERIVATIVE/CT
L57           5 SEA FILE=EMBASE ABB=ON  AMLODIPINE MALEATE/CT
L58        4062 SEA FILE=EMBASE ABB=ON  (L55 OR L56 OR L57) OR L5
L59        2021 SEA FILE=EMBASE ABB=ON  ATORVASTATIN/CT OR ATORVASTATIN
               LACTONE/CT OR ATORVASTATIN METHYL ESTER/CT
L60           1 SEA FILE=EMBASE ABB=ON  ATORVASTATINE/CT
L61        2021 SEA FILE=EMBASE ABB=ON  (L59 OR L60) OR L8
L62          87 SEA FILE=EMBASE ABB=ON  L58 AND L61
L63      223108 SEA FILE=EMBASE ABB=ON  DRUG COMBINATION/CT
L67       18660 SEA FILE=EMBASE ABB=ON  ANTIHYPERTENSIVE AGENT/CT
L68        8803 SEA FILE=EMBASE ABB=ON  BLOOD PRESSURE REGULATION/CT
L70      164593 SEA FILE=EMBASE ABB=ON  HYPERTENSION+NT/CT
L71       17568 SEA FILE=EMBASE ABB=ON  HYPERCHOLESTEROLEMIA+NT/CT
L72       33361 SEA FILE=EMBASE ABB=ON  HYPERLIPIDEMIA+NT/CT
L73       77985 SEA FILE=EMBASE ABB=ON  LIPID METABOLISM+NT/CT
L74       58314 SEA FILE=EMBASE ABB=ON  "DISORDERS OF LIPID AND LIPOPROTEIN
               METABOLISM"+NT/CT
L75        5965 SEA FILE=EMBASE ABB=ON  ANTILIPEMIC AGENT/CT
L78       34754 SEA FILE=EMBASE ABB=ON  DRUG MIXTURE/CT
L79          21 SEA FILE=EMBASE ABB=ON  L62 AND (L63 OR L78)
L80           7 SEA FILE=EMBASE ABB=ON  L79 AND (L67 OR L68 OR L70) AND ((L71
               OR L72 OR L73 OR L74 OR L75))
```

```
L3               STR
L5            62 SEA FILE=REGISTRY FAM FUL L3
L6               STR
L8            32 SEA FILE=REGISTRY FAM FUL L6
L55        4059 SEA FILE=EMBASE ABB=ON  AMLODIPINE/CT OR AMLODIPINE BESYLATE/CT

L56           1 SEA FILE=EMBASE ABB=ON  AMLODIPINE DERIVATIVE/CT
L57           5 SEA FILE=EMBASE ABB=ON  AMLODIPINE MALEATE/CT
L58        4062 SEA FILE=EMBASE ABB=ON  (L55 OR L56 OR L57) OR L5
L59        2021 SEA FILE=EMBASE ABB=ON  ATORVASTATIN/CT OR ATORVASTATIN
               LACTONE/CT OR ATORVASTATIN METHYL ESTER/CT
L60           1 SEA FILE=EMBASE ABB=ON  ATORVASTATINE/CT
L61        2021 SEA FILE=EMBASE ABB=ON  (L59 OR L60) OR L8
L62          87 SEA FILE=EMBASE ABB=ON  L58 AND L61
```

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L63      223108 SEA FILE=EMBASE ABB=ON  DRUG COMBINATION/CT
L66       12228 SEA FILE=EMBASE ABB=ON  CARDIOVASCULAR RISK/CT
L69      955876 SEA FILE=EMBASE ABB=ON  CARDIOVASCULAR DISEASE+NT/CT
L78       34754 SEA FILE=EMBASE ABB=ON  DRUG MIXTURE/CT
L79          21 SEA FILE=EMBASE ABB=ON  L62 AND (L63 OR L78)
L81           7 SEA FILE=EMBASE ABB=ON  L79 AND L66 AND L69


L55        4059 SEA FILE=EMBASE ABB=ON  AMLODIPINE/CT OR AMLODIPINE BESYLATE/CT

L56           1 SEA FILE=EMBASE ABB=ON  AMLODIPINE DERIVATIVE/CT
L57           5 SEA FILE=EMBASE ABB=ON  AMLODIPINE MALEATE/CT
L59        2021 SEA FILE=EMBASE ABB=ON  ATORVASTATIN/CT OR ATORVASTATIN
                LACTONE/CT OR ATORVASTATIN METHYL ESTER/CT
L60           1 SEA FILE=EMBASE ABB=ON  ATORVASTATINE/CT
L63      223108 SEA FILE=EMBASE ABB=ON  DRUG COMBINATION/CT
L78       34754 SEA FILE=EMBASE ABB=ON  DRUG MIXTURE/CT
L82        1513 SEA FILE=EMBASE ABB=ON  L55/MAJ OR L56/MAJ OR L57/MAJ
L83         714 SEA FILE=EMBASE ABB=ON  L59/MAJ OR L60/MAJ
L84           1 SEA FILE=EMBASE ABB=ON  L82 AND L83 AND (L63 OR L78)


=> s l65 or l80 or l81 or l84

L93          13 L65 OR L80 OR L81 OR L84

=> fil uspatf; d que nos l90

FILE 'USPATFULL' ENTERED AT 11:57:15 ON 26 FEB 2003
CA INDEXING COPYRIGHT (C) 2003 AMERICAN CHEMICAL SOCIETY (ACS)

FILE COVERS 1971 TO PATENT PUBLICATION DATE: 25 Feb 2003 (20030225/PD)
FILE LAST UPDATED: 25 Feb 2003 (20030225/ED)
HIGHEST GRANTED PATENT NUMBER: US6526583
HIGHEST APPLICATION PUBLICATION NUMBER: US2003037360
CA INDEXING IS CURRENT THROUGH 25 Feb 2003 (20030225/UPCA)
ISSUE CLASS FIELDS (/INCL) CURRENT THROUGH: 25 Feb 2003 (20030225/PD)
REVISED CLASS FIELDS (/NCL) LAST RELOADED: Dec 2002
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Dec 2002

>>>  USPAT2 is now available.  USPATFULL contains full text of the      <<<
>>>  original, i.e., the earliest published granted patents or          <<<
>>>  applications.  USPAT2 contains full text of the latest US          <<<
>>>  publications, starting in 2001, for the inventions covered in      <<<
>>>  USPATFULL.  A USPATFULL record contains not only the original      <<<
>>>  published document but also a list of any subsequent               <<<
>>>  publications.  The publication number, patent kind code, and       <<<
>>>  publication date for all the US publications for an invention      <<<
>>>  are displayed in the PI (Patent Information) field of USPATFULL    <<<
>>>  records and may be searched in standard search fields, e.g., /PN,  <<<
>>>  /PK, etc.                                                          <<<

>>>  USPATFULL and USPAT2 can be accessed and searched together         <<<
>>>  through the new cluster USPATALL.  Type FILE USPATALL to           <<<
>>>  enter this cluster.                                                <<<
>>>                                                                     <<<
>>>  Use USPATALL when searching terms such as patent assignees,        <<<
>>>  classifications, or claims, that may potentially change from       <<<
>>>  the earliest to the latest publication.                            <<<

This file contains CAS Registry Numbers for easy and accurate
substance identification.
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L3              STR
L5           62 SEA FILE=REGISTRY FAM FUL L3
L6              STR
L8           32 SEA FILE=REGISTRY FAM FUL L6
L85         141 SEA FILE=USPATFULL ABB=ON  L5
L86         146 SEA FILE=USPATFULL ABB=ON  (AMLODIPIN? OR NORVASC OR PELMEC)/IT
                ,TI,AB,CLM
L87         180 SEA FILE=USPATFULL ABB=ON  L8
L88         207 SEA FILE=USPATFULL ABB=ON  (ATORVASTATIN? OR CI981 OR CI 981
                OR ZARATOR OR LIPITOR OR YM 548 OR YM548)/IT,TI,AB,CLM
L89       62345 SEA FILE=USPATFULL ABB=ON  (SYNERG? OR INTERACT? OR POTENTIAT?)
                /IT,TI,AB,CLM
L90           9 SEA FILE=USPATFULL ABB=ON  (L85 OR L86) AND (L87 OR L88) AND
                L89


=> fil wpids; d que nos l100
FILE 'WPIDS' ENTERED AT 12:00:26 ON 26 FEB 2003
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FILE LAST UPDATED:          24 FEB 2003      <20030224/UP>
MOST RECENT DERWENT UPDATE:     200313        <200313/DW>
DERWENT WORLD PATENTS INDEX SUBSCRIBER FILE, COVERS 1963 TO DATE

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>>> PATENT IMAGES AVAILABLE FOR PRINT AND DISPLAY >>>

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    SEE http://www.derwent.com/dwpi/updates/dwpicov/index.html <<<

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 http://www.stn-international.de/training_center/patents/stn_guide.pdf <<<

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    GUIDES, PLEASE VISIT:
    http://www.derwent.com/userguides/dwpi_guide.html <<<


L95         189 SEA FILE=WPIDS ABB=ON  (ATORVASTATIN? OR CI981 OR CI 981 OR
                ZARATOR OR LIPITOR OR YM 548 OR YM548)
L96         133 SEA FILE=WPIDS ABB=ON  (AMLODIPIN? OR NORVASC OR PELMEC)
L97      145216 SEA FILE=WPIDS ABB=ON  (SYNERG? OR INTERACT? OR POTENTIAT?)
L100          5 SEA FILE=WPIDS ABB=ON  L95 AND L96 AND L97


=> DUP REM L92 L91 L93 L90 l100
FILE 'MEDLINE' ENTERED AT 12:00:39 ON 26 FEB 2003

FILE 'HCAPLUS' ENTERED AT 12:00:39 ON 26 FEB 2003
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FILE 'EMBASE' ENTERED AT 12:00:39 ON 26 FEB 2003

FILE 'USPATFULL' ENTERED AT 12:00:39 ON 26 FEB 2003

FILE 'WPIDS' ENTERED AT 12:00:39 ON 26 FEB 2003

PROCESSING COMPLETED FOR L92
PROCESSING COMPLETED FOR L91
PROCESSING COMPLETED FOR L93
PROCESSING COMPLETED FOR L90
PROCESSING COMPLETED FOR L100
L101 40 DUP REM L92 L91 L93 L90 L100 (5 DUPLICATES REMOVED)
ANSWER '1' FROM FILE MEDLINE
ANSWERS '2-17' FROM FILE HCAPLUS
ANSWERS '18-30' FROM FILE EMBASE
ANSWERS '31-38' FROM FILE USPATFULL
ANSWERS '39-40' FROM FILE WPIDS

=> d ibib ab hitrn 1-40; fil hom

L101 ANSWER 1 OF 40 MEDLINE DUPLICATE 3
ACCESSION NUMBER: 2002441054 MEDLINE
DOCUMENT NUMBER: 22114271 PubMed ID: 12119194
TITLE: Raman spectroscopic investigation of **atorvastatin**, amlodipine, and both on atherosclerotic plaque development in APOE*3 Leiden transgenic mice.
AUTHOR: van de Poll Sweder W E; Delsing Dianne J M; Jukema J Wouter; Princen Hans M G; Havekes Louis M; Puppels Gerwin J; van der Laarse Arnoud
CORPORATE SOURCE: Department of Cardiology, C5-P, Leiden University Medical Center, P.O. Box 9600, 2300 RC, Leiden, The Netherlands.
SOURCE: ATHEROSCLEROSIS, (2002 Sep) 164 (1) 65-71.
Journal code: 0242543. ISSN: 0021-9150.
PUB. COUNTRY: Ireland
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200211
ENTRY DATE: Entered STN: 20020830
Last Updated on STN: 20021214
Entered Medline: 20021126

Bad Date

AB Raman spectroscopy allows quantitative, non-destructive evaluation of entire, intact atherosclerotic plaques. We quantified the anti-atherosclerotic effects of **atorvastatin** and amlodipine on progression of atherosclerosis using post-mortem Raman spectroscopic plaque imaging in 28 APOE*3 Leiden transgenic mice who were fed a high fat/high cholesterol diet for 28 weeks. Mice were assigned to a control group receiving the diet alone or to groups that received the diet with either 0.01% w/w **atorvastatin**, 0.002% w/w amlodipine, or the combination. The entire excised aortic arch was scanned with Raman microspectroscopy for quantitation of the distribution of cholesterol and calcification content. When mice had been treated with **atorvastatin**, cholesterol accumulation and calcification in the aortic arch was reduced by 91 and 98%, respectively, (both $P<0.001$). Amlodipine did not reduce the cholesterol content but reduced calcification of the aorta by 69% ($P<0.05$). The combination of amlodipine and **atorvastatin** was as effective as **atorvastatin** alone. This study demonstrates the strong atheroprotective potential of **atorvastatin**. In addition it is demonstrated that amlodipine reduces mineralization of atherosclerotic plaque. No synergistic effect of the combination of amlodipine and **atorvastatin** on plaque

development is demonstrated. This study encourages Raman spectroscopic evaluations of anti-atherosclerotic drugs in larger animals and humans in vivo.

L101 ANSWER 2 OF 40 HCAPLUS COPYRIGHT 2003 ACS DUPLICATE 1
ACCESSION NUMBER: 2002:122785 HCAPLUS
DOCUMENT NUMBER: 136:161369
TITLE: **Synergistic** effect of **amlodipine** and **atorvastatin**
INVENTOR(S): Mason, R. Preston
PATENT ASSIGNEE(S): USA
SOURCE: PCT Int. Appl., 45 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002011723	A1	20020214	WO 2001-US24209	20010803
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2001083085	A5	20020218	AU 2001-83085	20010803
US 2002052394	A1	20020502	US 2001-921479	20010803

PRIORITY APPLN. INFO.: US 2000-223214P P 20000804
WO 2001-US24209 W 20010803

AB The combination of the **antihypertensive** calcium channel blocker amlodipine and lipid-lowering agent atorvastatin inhibits free cholesterol crystn. in **atherosclerotic**-like membranes. In addn., treatment with a combination of amlodipine and atorvastatin results in a **synergistic** effect on the release of NO from rabbit aorta endothelial cells.

IT **88150-42-9, Amlodipine 88150-42-9D, Amlodipine**, derivs. **111470-99-6, Amlodipine** besylate **134523-00-5, Atorvastatin 134523-00-5D, Atorvastatin**, hydroxylated metabolites and derivs. **134523-03-8, Atorvastatin** hemicalcium
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**amlodipine-atorvastatin synergistic** effect on inhibition of cholesterol crystn. and on NO release in endothelial cells)

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L101 ANSWER 3 OF 40 HCAPLUS COPYRIGHT 2003 ACS DUPLICATE 2
ACCESSION NUMBER: 2002:505413 HCAPLUS
DOCUMENT NUMBER: 137:57567
TITLE: **Synergistic** effects of **amlodipine** and **atorvastatin** metabolite as a basis for combination antioxidant therapy, and use in the treatment of cardiovascular disease
INVENTOR(S): Mason, R. Preston
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 23 pp., Cont.-in-part of U. S.

Searched by Barb O'Bryen, STIC 308-4291

Ser. No. 556,930, abandoned.
CODEN: USXXCO

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002086889	A1	20020704	US 2001-33149	20011019

PRIORITY APPLN. INFO.:
US 1999-130665P P 19990423
US 1999-145305P P 19990723
US 1999-151121P P 19990827
US 1999-166592P P 19991119
US 2000-556930 B2 20000421

AB The combination of amlodipine with atorvastatin metabolite shows a **synergistic** antioxidant effect on lipid peroxidn. in human low-d. lipoproteins and membrane vesicles enriched with polyunsatd. fatty acids. Inhibition of oxy-radical damage by this drug combination was obsd. at therapeutic levels in a manner that could not be reproduced by the combination of amlodipine with other statins or the natural antioxidant, vitamin E. The basis for this potent activity is attributed to the chem. structures of these compds. and their mol. **interactions** with phospholipid mols., as detd. by x-ray diffraction analyses. This combination therapy can be used to treat cardiovascular disorders, esp. coronary artery disease, by increasing the resistance of low-d. lipoproteins and vascular cell membranes against oxidative modification.

IT **88150-42-9, Amlodipine 134523-00-5D,**
Atorvastatin, hydroxylated metabolites
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**amlodipine-atorvastatin** metabolite **synergistic** antioxidant combination, and use in treatment of cardiovascular disease)

IT **88150-42-9D, Amlodipine,** derivs. **111470-99-6,**
Amlodipine besylate
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**amlodipine-atorvastatin** metabolite **synergistic** antioxidant combination, and use in treatment of cardiovascular disease)

L101 ANSWER 4 OF 40 HCAPLUS COPYRIGHT 2003 ACS DUPLICATE 4
ACCESSION NUMBER: 2000:772453 HCAPLUS
DOCUMENT NUMBER: 133:305601
TITLE: **Synergistic** antioxidant effects of **amlodipine** and **atorvastatin,** and therapeutic use in cardiovascular disease
INVENTOR(S): Mason, R. Preston
PATENT ASSIGNEE(S): USA
SOURCE: PCT Int. Appl., 79 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000064443	A1	20001102	WO 2000-US10465	20000418
WO 2000064443	C2	20020829		

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS,

JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

EP 1173172	A1	20020123	EP 2000-928200	20000418
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
BR 2000010689	A	20020219	BR 2000-10689	20000418
JP 2002542289	T2	20021210	JP 2000-613434	20000418
NO 2001005128	A	20011220	NO 2001-5128	20011019

PRIORITY APPLN. INFO.:

US 1999-130665P	P	19990423
US 1999-145305P	P	19990723
US 1999-151121P	P	19990827
US 1999-166592P	P	19991119
WO 2000-US10465	W	20000418

AB The combination of amlodipine with either atorvastatin or atorvastatin metabolite shows a **synergistic** antioxidant effect on lipid peroxidn. in human low-d. lipoproteins and membrane vesicles enriched with polyunsatd. fatty acids. Inhibition of oxy-radical damage by this drug combination was obsd. at therapeutic levels in a manner that could not be reproduced by the combination of amlodipine with other statins or the natural antioxidant, vitamin E. The basis for this potent activity is attributed to the chem. structures of these compds. and their mol. **interactions** with phospholipid mols., as detd. by x-ray diffraction analyses. This combination therapy can be used to treat cardiovascular disorders, esp. coronary artery disease, by increasing the resistance of low-d. lipoproteins and vascular cell membranes against oxidative modification.

IT **88150-42-9, Amlodipine**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**synergistic** antioxidant effects of **amlodipine** and **atorvastatin**, and therapeutic use in cardiovascular disease)

IT **88150-42-9D, Amlodipine**, derivs. **111470-99-6, Amlodipine** besylate **134523-00-5, Atorvastatin** **134523-00-5D, Atorvastatin**, derivs. and hydroxylated metabolites **134523-03-8, Atorvastatin** calcium
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**synergistic** antioxidant effects of **amlodipine** and **atorvastatin**, and therapeutic use in cardiovascular disease)

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L101 ANSWER 5 OF 40 HCAPLUS COPYRIGHT 2003 ACS DUPLICATE 5
ACCESSION NUMBER: 1999:184129 HCAPLUS
DOCUMENT NUMBER: 130:205138
TITLE: Therapeutic combinations comprising **amlodipine** and **atorvastatin**
INVENTOR(S): Buch, Jan; Scott, Robert Andrew Donald
PATENT ASSIGNEE(S): Pfizer Inc., USA
SOURCE: PCT Int. Appl., 50 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9911259	A1	19990311	WO 1998-IB1225	19980811
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2301732	AA	19990311	CA 1998-2301732	19980811
AU 9885548	A1	19990322	AU 1998-85548	19980811
EP 1003503	A1	20000531	EP 1998-936587	19980811
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, LT, LV, FI, RO				
BR 9812030	A	20000926	BR 1998-12030	19980811
JP 2001514222	T2	20010911	JP 2000-508362	19980811
ZA 9807844	A	20000228	ZA 1998-7844	19980828
US 6455574	B1	20020924	US 2000-512914	20000225
NO 2000000998	A	20000228	NO 2000-998	20000228
US 2003008904	A1	20030109	US 2002-214058	20020807

PRIORITY APPLN. INFO.: US 1997-57275P P 19970829
WO 1998-IB1225 W 19980811
US 2000-512914 A3 20000225

AB This invention relates to pharmaceutical combinations of amlodipine or a pharmaceutically acceptable acid addn. salt thereof and atorvastatin or a pharmaceutically acceptable salt thereof, kits contg. such combinations and methods of using such combinations to treat subjects suffering from angina pectoris, **atherosclerosis**, combined **hypertension** and hyperlipidemia and to treat subjects presenting with symptoms of cardiac risk, including humans. This invention also relates to additive and **synergistic** combinations of amlodipine and atorvastatin whereby those **synergistic** combinations are useful in treating subjects suffering from angina pectoris, **atherosclerosis**, combined **hypertension** and hyperlipidemia and those subjects presenting with symptoms of cardiac risk, including humans.

IT **88150-42-9, Amlodipine 111470-99-6, Amlodipine** besylate **134523-00-5, Atorvastatin 134523-03-8, Atorvastatin** calcium
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**antihypertensive** and antihyperlipidemic compns. contg. **amlodipine** and **atorvastatin**)

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L101 ANSWER 6 OF 40 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:927184 HCAPLUS
DOCUMENT NUMBER: 138:14048
TITLE: Preparation of oxazolylethoxyphenylprolines and related compounds as antidiabetic and antiobesity agents.
INVENTOR(S): Cheng, Peter T.; Jeon, Yoon; Wang, Wei
PATENT ASSIGNEE(S): Bristol-Myers Squibb Company, USA
SOURCE: PCT Int. Appl., 107 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002096357	A2	20021205	WO 2002-US16628	20020523

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2001-294505P P 20010530

OTHER SOURCE(S): MARPAT 138:14048

AB Title compds. [I; m, n = 0-2; Q = C, N; A = (CH2)x, (CH2)x1, with an alkenyl or alkynyl bond in the chain, (CH2)x2O(CH2)x3; x = 1-5; x1 = 2-5; x2, x3 = 0-5; provided that .gtoreq.1 of x2 and x3 .noteq. 0; X1 = CH, N; X2 = C, N, O, S; X3 = C, N; X4 = C, N, O, S provided that .gtoreq.1 of X2, X3, X4 = N; in each of X1-X4, C may include CH; R1 = H, alkyl; R2 = H, alkyl, alkoxy, halo, (substituted) amino; R2a, R2b R2c = H, alkyl, alkoxy, halo, (substituted) amino; R3 = H, alkyl, arylalkyl, aryloxycarbonyl, alkyloxycarbonyl, alkynyloxycarbonyl, alkenyloxycarbonyl, arylcarbonyl, alkylcarbonyl, aryl, heteroaryl, cycloheteroalkyl, heteroarylcarbonyl, heteroarylheteroarylalkyl, alkylcarbonylamino, arylcarbonylamino, heteroarylcarbonylamino, alkoxycarbonylamino, aryloxycarbonylamino, heteroaryloxycarbonylamino, heteroarylheteroarylcarbonyl, alkylsulfonyl, alkenylsulfonyl, heteroaryloxycarbonyl, cycloheteroalkyloxycarbonyl, aryloxyheteroarylalkyl, heteroarylalkyloxyarylalkyl, arylarylalkyl, arylalkenylarylalkyl, arylaminoarylalkyl, etc.; Y = CO2R4, 1-tetrazolyl, P(O)(OR4a)R5, P(O)(OR4a)2; R4 = H, alkyl, prodrug ester; R4a = H, prodrug ester; R5 = alkyl, aryl; Z = (CH2)x4, (CH2)x5, (CH2)x6O(CH2)x7; x4 = 1-5; x5 = 2-5; x6, x7 = 0-4], were prepd. as antidiabetic and antiobesity agents (no data). Thus, title compd. (II) was prepd. in 6 steps.

IT **111470-99-6, Amlodipine** besylate **134523-00-5, Atorvastatin**

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (coadministration; prepn. of oxazolylethoxyphenylprolines and related compds. as antidiabetic and antiobesity agents)

L101 ANSWER 7 OF 40 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2002:540258 HCAPLUS

DOCUMENT NUMBER: 137:109267

TITLE: Preparation of benzoxepinopyridines as HMG-CoA reductase inhibitors

INVENTOR(S): Robl, Jeffrey A.; Chen, Bang-chi; Sun, Chong-qing

PATENT ASSIGNEE(S): USA

SOURCE: U.S. Pat. Appl. Publ., 42 pp., Cont.-in-part of U.S. Ser. No. 875,155.
CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002094977	A1	20020718	US 2001-7407	20011204
US 2002013334	A1	20020131	US 2001-875155	20010606

PRIORITY APPLN. INFO.: US 2000-211595P P 20000615
US 2001-875155 A2 20010606

OTHER SOURCE(S): MARPAT 137:109267

AB Title compds. I [X = O, S, SO, SO2, NR7; Z = HOCHCH2CH(OH)CH2CO2R3,

4-hydroxy-2-oxopyran-6-yl, etc.; n = 0, 1; R1, R2 = alkyl, arylalkyl, cycloalkyl, alkenyl, cycloalkenyl, aryl, heteroaryl, cycloheteroalkyl; R3 = H, alkyl, metal ion; R4 = H, halo, CF3, etc.; R7 = H, alkyl, aryl, alkanoyl, aroyl, alkoxycarbonyl, etc.; R9, R10 = H, alkyl], were prepd. as HMG CoA reductase inhibitors active in inhibiting cholesterol biosynthesis, modulating blood serum lipids such as lowering LDL cholesterol and/or increasing HDl cholesterol, and treating hyperlipidemia, hypercholesterolemia, hypertriglyceridemia and **atherosclerosis** (no data). E.g., a multistep synthesis of II is reported.

IT **134523-00-5, Atorvastatin 246852-12-0, Amlodipine** mesylate
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(coadministered agents; prepn. of benzoxepinopyridines as HMG-CoA reductase inhibitors for the treatment of hyperlipidemia, hypercholesterolemia, hypertriglyceridemia, **atherosclerosis**, and other disorders)

L101 ANSWER 8 OF 40 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:392237 HCAPLUS
DOCUMENT NUMBER: 136:401651
TITLE: Preparation of fused pyridine derivatives as HMG-CoA reductase inhibitors
INVENTOR(S): Robl, Jeffrey A.; Chen, Bang-Chi; Sun, Chong-Qing
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 46 pp., Cont.-in-part of U.S. Ser. No. 875,218.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002061901	A1	20020523	US 2001-8154	20011204
US 2002028826	A1	20020307	US 2001-875218	20010606

PRIORITY APPLN. INFO.: US 2000-211594P P 20000615
US 2001-875218 A2 20010606
OTHER SOURCE(S): MARPAT 136:401651

AB The title compds. I and their pharmaceutically acceptable salts, esters, prodrug esters, and stereoisomers are claimed [wherein: Z = CH(OH)CH2CR7(OH)CH2CO2R3 or corresponding pyranone lactone derivs.; n = 0, 1; x = 0, 1, 2, 3, or 4; y = 0, 1, 2, 3 or 4, provided that at least one of x and y is other than 0; and optionally one or more carbons of (CH2)x and/or (CH2)y together with addnl. carbons form a 3 to 7 membered spirocyclic ring; R1, R2 = alkyl, arylalkyl, cycloalkyl, alkenyl, cycloalkenyl, aryl, heteroaryl, cycloheteroalkyl; R3 = H or lower alkyl; R4 = H, halo, CF3, OH, alkyl, alkoxy, CO2H, (un)substituted NH2, cyano, (un)substituted CONH2, etc.; R7 = H, alkyl]. The compds. are HMG-CoA reductase inhibitors, and are active in inhibiting cholesterol biosynthesis and modulating blood serum lipids, for example, lowering LDL cholesterol and/or increasing HDL cholesterol (no data). I are thus useful in treating hyperlipidemia and dyslipidemia, in hormone replacement therapy, and in treating hypercholesterolemia, hypertriglyceridemia and **atherosclerosis**, as well as Alzheimer's disease and osteoporosis. Prepns. of several compds. are described. For instance, a multistep synthesis of fused pyridine deriv. II is reported. Compds. I may be used in a manner similar to atorvastatin, pravastatin, simvastatin, etc. Combinations of compds. I with various other drugs are claimed, the latter being specified as certain pharmacol. classes, as inhibitors of specific enzymes, as (ant)agonists of specific receptors, and as numerous named

drugs.

IT **111470-99-6, Amlodipine** besylate **134523-00-5, Atorvastatin**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(therapeutic compns. also contg.; prepn. of fused pyridine derivs. as HMG-CoA reductase inhibitors)

L101 ANSWER 9 OF 40 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:364016 HCAPLUS
DOCUMENT NUMBER: 136:369612
TITLE: Preparation of an **amlodipine/atorvastatin** amide prodrug for the treatment of **atherosclerosis**, angina pectoris, **hypertension**, hyperlipidemia and management of cardiac risk.
INVENTOR(S): Crook, Robert J.; Pettman, Alan J.
PATENT ASSIGNEE(S): Pfizer Limited, UK; Pfizer Inc.
SOURCE: Eur. Pat. Appl., 21 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1205477	A1	20020515	EP 2001-309169	20011030
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
US 2002082282	A1	20020627	US 2001-985	20011031
BR 2001005080	A	20020625	BR 2001-5080	20011108
JP 2002179675	A2	20020626	JP 2001-344576	20011109

PRIORITY APPLN. INFO.: GB 2000-27410 A 20001109
US 2000-255025P P 20001212
OTHER SOURCE(S): CASREACT 136:369612

AB The present invention discloses the prepn. of an amide-linked amlodipine/atorvastatin prodrug I and pharmaceutically acceptable acid addn. salts [wherein: R = H with (R), (S), or (R/S) stereochem.]. For example, a soln. of R(-)-amlodipine (2 mmol) and atorvastatin lactone II (1.8 mmol) in ethanol (30 mL) was refluxed for 18 h. The solvent was then evapd. in vacuo and the resulting oil purified by column chromatog. to provide the prodrug I [R = (R)-H] as a white foam in 76% yield. Hydrolytic cleavage of the prodrug amide bond provides amlodipine and atorvastatin in vivo. Methods for clin. study of I in the treatment of **atherosclerosis**, angina pectoris, **hypertension**, hyperlipidemia and management of cardiac risk are described (no data).

IT **88150-42-9, Amlodipine 111470-99-6, Amlodipine** besylate **134523-03-8, Atorvastatin** hemicalcium salt
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(compns. contg.; prepn. of an **amlodipine/atorvastatin** amide prodrug)

IT **103129-81-3 103129-82-4**
RL: RCT (Reactant); RACT (Reactant or reagent)
(precursor; prepn. of an **amlodipine/atorvastatin** amide prodrug)

IT **134523-00-5, Atorvastatin**
RL: RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); RACT (Reactant or reagent); USES (Uses)
(precursor; prepn. of an **amlodipine/atorvastatin** amide prodrug)

REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L101 ANSWER 10 OF 40 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:886157 HCAPLUS
DOCUMENT NUMBER: 136:11105
TITLE: Cobalamin compounds useful as cardiovascular agents and as imaging agents
INVENTOR(S): Collins, Douglas A.; Hogenkamp, Henricus P. C.
PATENT ASSIGNEE(S): Mayo Foundation for Medical Education and Research, USA; Regents of the University of Minnesota
SOURCE: PCT Int. Appl., 158 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001092283	A2	20011206	WO 2001-US17694	20010531
WO 2001092283	A3	20020704		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

US 2002049155	A1	20020425	US 2001-873142	20010531

PRIORITY APPLN. INFO.: US 2000-208140P P 20000531
US 2001-267782P P 20010209

OTHER SOURCE(S): MARPAT 136:11105
AB The invention provides cobalamin derivs. linked to a cardiovascular agent, as well as pharmaceutical compns. comprising the compds. and methods for using the compds. in treatment or diagnosis of a cardiovascular disease.
IT **111470-99-6D**, **Norvasc**, cobalamin conjugates
134523-03-8D, **Lipitor**, cobalamin conjugates
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cobalamin compds. useful as cardiovascular agents and as imaging agents)

L101 ANSWER 11 OF 40 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:780643 HCAPLUS
DOCUMENT NUMBER: 135:335144
TITLE: **Drug delivery** system for avoiding pharmacokinetic **interaction** between **drugs** and method thereof
INVENTOR(S): Sawada, Toyohiro; Sako, Kazuhiro; Yoshioka, Tatsunobu; Watanabe, Shunsuke
PATENT ASSIGNEE(S): Yamanouchi Pharmaceutical Co., Ltd., Japan
SOURCE: PCT Int. Appl., 44 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001078681	A1	20011025	WO 2001-JP3228	20010416

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM,

HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

US 2002022054 A1 20020221 US 2001-834414 20010412
EP 1275373 A1 20030115 EP 2001-923966 20010416
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
PRIORITY APPLN. INFO.: US 2000-197574P P 20000417
WO 2001-JP3228 W 20010416

AB Disclosed a system for avoiding an unfavorable pharmacokinetic interaction between a drug and another concomitant drug which comprises controlling the release time and/or release site of the drug and/or the concomitant drug in the body. A controlled-release tablet of conivaptan hydrochloride was prepd. and applied to a dog with midazolam oral liq. to examine the blood concn. of midazolam. The obtained conivaptan tablet showed no effect on metab. of midazolam through drug metabolizing enzyme CYP3A4.

IT **88150-42-9, Amlodipine 134523-00-5, Atorvastatin**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**drug** delivery system for avoiding pharmacokinetic **interaction** between **drugs** and method thereof)

REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L101 ANSWER 12 OF 40 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:747597 HCAPLUS
DOCUMENT NUMBER: 135:267248
TITLE: Vasopeptidase inhibitors, alone or with other agents, for the treatment of isolated systolic hypertension
INVENTOR(S): Reeves, Richard A.; Wolf, Robert A.; Chang, Paul I.
PATENT ASSIGNEE(S): Bristol-Myers Squibb Co., USA
SOURCE: PCT Int. Appl., 16 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001074348	A2	20011011	WO 2001-US8240	20010315

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

EP 1267855 A2 20030102 EP 2001-964664 20010315
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
US 2002004500 A1 20020110 US 2001-819549 20010328
PRIORITY APPLN. INFO.: US 2000-194499P P 20000403
WO 2001-US8240 W 20010315

AB Vasopeptidase inhibitors, esp. omapatrilat, are useful in treating isolated systolic hypertension. The vasopeptidase inhibitor may be used in combination with other pharmaceutically active agents.

IT **111470-99-6, Amlodipine** besylate **134523-03-8, Atorvastatin** calcium
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(vasopeptidase inhibitors, alone or with other agents, for treatment of isolated systolic hypertension)

L101 ANSWER 13 OF 40 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:338762 HCAPLUS
DOCUMENT NUMBER: 134:362292
TITLE: Methods of determining individual hypersensitivity to a pharmaceutical agent from gene expression profile
INVENTOR(S): Farr, Spencer
PATENT ASSIGNEE(S): Phase-1 Molecular Toxicology, USA
SOURCE: PCT Int. Appl., 222 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001032928	A2	20010510	WO 2000-US30474	20001103
WO 2001032928	A3	20020725		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 1999-165398P P 19991105
US 2000-196571P P 20000411

AB The invention discloses methods, gene databases, gene arrays, protein arrays, and devices that may be used to det. the hypersensitivity of individuals to a given agent, such as drug or other chem., in order to prevent toxic side effects. In one embodiment, methods of identifying hypersensitivity in a subject by obtaining a gene expression profile of multiple genes assocd. with hypersensitivity of the subject suspected to be hypersensitive, and identifying in the gene expression profile of the subject a pattern of gene expression of the genes assocd. with hypersensitivity are disclosed. The gene expression profile of the subject may be compared with the gene expression profile of a normal individual and a hypersensitive individual. The gene expression profile of the subject that is obtained may comprise a profile of levels of mRNA or cDNA. The gene expression profile may be obtained by using an array of nucleic acid probes for the plurality of genes assocd. with hypersensitivity. The expression of the genes predetd. to be assocd. with hypersensitivity is directly related to prevention or repair of toxic damage at the tissue, organ or system level. Gene databases arrays and app. useful for identifying hypersensitivity in a subject are also disclosed.

IT **88150-42-9, Amlodipine 134523-00-5, Atorvastatin**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(methods of detg. individual hypersensitivity to a pharmaceutical agent from gene expression profile)

L101 ANSWER 14 OF 40 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:283949 HCAPLUS
DOCUMENT NUMBER: 134:311218
TITLE: Synthesis and use of heterocyclic sodium/proton exchange inhibitors
INVENTOR(S): Ahmad, Saleem; Wu, Shung C.; O'Neil, Steven V.; Ngu, Khehyong; Atwal, Karnail S.
PATENT ASSIGNEE(S): Bristol-Myers Squibb Company, USA
SOURCE: PCT Int. Appl., 221 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001027107	A2	20010419	WO 2000-US27461	20001002
WO 2001027107	A3	20020124		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

EP 1224183	A2	20020724	EP 2000-968723	20001002
NO 2002001717	A	20020610	NO 2002-1717	20020411

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL

PRIORITY APPLN. INFO.:
US 1999-158755P P 19991012
WO 2000-US27461 W 20001002

OTHER SOURCE(S): MARPAT 134:311218

AB Compds. of formula I [wherein; n is 1-5; X is N or CR5, where R5 is H, halo, alkenyl, alkynyl, alkoxy, alkyl, aryl or heteroaryl; Z is a heteroaryl group; R1 is H, alk(en)(yn)yl, alk(enyl)(ynyl)oxy, (aryl or alkyl)3Si, cycloalk(en)yl, (aryl)amino, aryl(alkyl), cycloheteroaryl, etc.; R2, R3 and R4 are any of the groups set out for R1 and optionally substituted with 1 to 5 substituents which may be the same or different and when X is N, R1 is preferably aryl or heteroaryl] are claimed. Several hundred examples are disclosed. Synthesis of II proceeds via cyclopropanation of the cinnamate derived from the olefination between 3,5-dichlorobenzaldehyde and t-butyldiethylphosphonoacetate. The intermediate tert-Bu ester is converted to the corresponding .alpha.-chloroketone and reacted with acetyl guanidine to provide II in a total of 5 steps. Compds. I are said to be sodium/proton exchange inhibitors (NHE). Pharmaceutical combinations are claimed using I and certain **antihypertensive** agents, .beta.-adrenergic agonists, hypolipidemic agents, antidiabetic agents, antiobesity agents, etc. Compds. I are useful as antianginal and cardioprotective agents and provide a method for preventing or treating angina pectoris, cardiac dysfunction, myocardial necrosis, and arrhythmia.

IT **111470-99-6**, **Amlodipine** besylate **134523-00-5**, **Atorvastatin**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceuticals also contg.; synthesis and use of heterocyclic sodium/proton exchange inhibitors)

L101 ANSWER 15 OF 40 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2001:732085 HCAPLUS
DOCUMENT NUMBER: 136:31286
TITLE: Population pharmacokinetics of everolimus in de novo renal transplant patients: impact of ethnicity and comedications
AUTHOR(S): Kovarik, John M.; Hsu, Chyi-Hung; McMahon, Louis; Berthier, Stephane; Rordorf, Christiane
CORPORATE SOURCE: Novartis Pharmaceuticals, Basel, 4002, Switz.
SOURCE: Clinical Pharmacology & Therapeutics (St. Louis, MO, United States) (2001), 70(3), 247-254
CODEN: CLPTAT; ISSN: 0009-9236
PUBLISHER: Mosby, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Everolimus is a macrolide immunosuppressant intended for acute rejection prophylaxis after kidney transplantation. A total of 5260 blood samples were collected in the context of two randomized, double-blind, multicenter efficacy trials in 673 patients over a 6-mo period after kidney transplantation. The data were evaluated in a nonlinear mixed-effects model. The influence of demog. characteristics (age, wt., sex, and ethnicity) and of comedications on everolimus exposure was explored. For a ref. 44-yr-old, 71-kg Caucasian kidney allograft recipient receiving everolimus as part of a cyclosporine (INN, cyclosporin)-prednisone immunosuppressive regimen, the absorption rate const. was 6.07 h-1 (std. error [SE], 0.70 h-1), the apparent clearance was 8.8 L/h (SE, 0.2 L/h), and the apparent central distribution vol. was 110 L (SE, 5 L). There were no clin. relevant influences of age, wt., or sex on clearance. No significant difference in clearance was detected for Asian patients, whereas black patients had an av. clearance that was 20% higher than that of nonblack patients. Patients concomitantly receiving erythromycin or azithromycin had an av. 19% lower clearance. One patient receiving itraconazole had a 74% redn. in clearance. After we accounted for covariates, the remaining interindividual variability in clearance was 27% and the variability for distribution vol. was 36%. The combined intraindividual and assay/measurement residual error in everolimus blood concns. was 31%. Dose adjustment of everolimus on the basis of wt. does not appear necessary. Black patients may need a higher dose to achieve exposure that is similar to that of nonblack patients. Concomitant administration of potent inhibitors of the cytochrome P 450 isoenzyme CYP3A may reduce everolimus clearance and increase its blood concns.

IT **88150-42-9, Amlodipine 134523-00-5, Atorvastatin**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(population pharmacokinetics of everolimus in de novo renal transplant humans and impact of ethnicity and comedications)

REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L101 ANSWER 16 OF 40 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2000:861673 HCAPLUS
DOCUMENT NUMBER: 134:29248
TITLE: Preparation and uses of mutual prodrugs of **amlodipine** and **atorvastatin**
INVENTOR(S): Chang, George; Hamanaka, Ernest Seiichi; Lamattina, John Lawrence
PATENT ASSIGNEE(S): Pfizer Products Inc., USA
SOURCE: PCT Int. Appl., 33 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

Searched by Barb O'Bryen, STIC 308-4291

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000073298	A1	20001207	WO 2000-IB313	20000320
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
BR 2000011006	A	20020219	BR 2000-11006	20000320
EP 1180102	A1	20020220	EP 2000-911145	20000320
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2003500487	T2	20030107	JP 2000-621364	20000320
US 6486182	B1	20021126	US 2000-577561	20000524
NO 2001005756	A	20020124	NO 2001-5756	20011126

PRIORITY APPLN. INFO.: US 1999-136608P P 19990527
WO 2000-IB313 W 20000320

OTHER SOURCE(S): MARPAT 134:29248

AB This invention relates to mutual prodrugs of amlodipine and atorvastatin, e.g. I and II (R1 = R2 = H; R1, R2 = H, C1-4-alkyl), and to pharmaceutical compns. thereof. Thus, II (R1 = R2 = H) was prepd. via reaction of amlodipine with ClCO2CH2Cl in CHCl3 contg. pyridine followed by reaction with atorvastatin calcium salt in DMF. This invention also relates to methods of treating angina pectoris, **atherosclerosis**, and **hypertension** and hyperlipidemia in a mammal using those prodrugs and compns. and to methods of managing cardiac risk in a mammal, including humans, presenting with symptoms of cardiac risk by administering those prodrugs and compns.

IT **88150-42-9, Amlodipine 103129-81-3**, (R)-**Amlodipine 103129-82-4**, (S)-**Amlodipine 134523-00-5, Atorvastatin**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); RACT (Reactant or reagent); USES (Uses)
(prepn. and uses mutual of prodrugs of **amlodipine** and **atorvastatin**)

IT **88150-42-9DP, Amlodipine**, mutual prodrugs with **atorvastatin 134523-00-5DP, Atorvastatin**, mutual prodrugs with **amlodipine**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. and uses mutual of prodrugs of **amlodipine** and **atorvastatin**)

IT **111470-99-6, Amlodipine** besylate **134523-03-8, Atorvastatin** calcium
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(prepn. and uses mutual of prodrugs of **amlodipine** and **atorvastatin**)

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L101 ANSWER 17 OF 40 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2000:861653 HCAPLUS
DOCUMENT NUMBER: 134:21483
TITLE: Mutual salt of **amlodipine** and

Searched by Barb O'Bryen, STIC 308-4291

atorvastatin

INVENTOR(S): Chang, George; Hamanaka, Ernest Seiichi
PATENT ASSIGNEE(S): Pfizer Products Inc., USA
SOURCE: PCT Int. Appl., 27 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000073271	A1	20001207	WO 2000-IB590	20000508
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
BR 2000011008	A	20020219	BR 2000-11008	20000508
EP 1180097	A1	20020220	EP 2000-920978	20000508
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2003500473	T2	20030107	JP 2000-621338	20000508
US 6262092	B1	20010717	US 2000-578204	20000524
NO 2001005757	A	20011220	NO 2001-5757	20011126

PRIORITY APPLN. INFO.: US 1999-136269P P 19990527
WO 2000-IB590 W 20000508

AB This invention relates to a mutual salt of amlodipine and atorvastatin, pharmaceutical compns. and methods of treating angina pectoris, **atherosclerosis** and combined **hypertension** and hyperlipidemia in mammals with such a mutual salt. This invention also relates to methods of managing cardiac risk in a mammal presenting with symptoms of cardiac risk, including humans by administering such a mutual salt and compns. Thus, a free acid of atorvastatin in EtOAc soln. was added to the free base of racemic amlodipine to give the diastereomeric salt of the 2 drugs.

IT **134523-03-8, Atorvastatin** hemicalcium
RL: RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); RACT (Reactant or reagent); USES (Uses)
(mutual salt of **amlodipine** and **atorvastatin**)

IT **309940-12-3P**
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(mutual salt of **amlodipine** and **atorvastatin**)

IT **88150-42-9, Amlodipine 111470-99-6, Amlodipine** besylate **134523-00-5, Atorvastatin**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(mutual salt of **amlodipine** and **atorvastatin**)

IT **309940-13-4P**
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of mutual salt of **amlodipine** and **atorvastatin**)

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L101 ANSWER 18 OF 40 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2002339315 EMBASE
TITLE: Case 2: Strategies to minimize the use of calcineurin

inhibitors (CNIs).
AUTHOR: Hariharan S.
SOURCE: Transplantation, (15 Sep 2002) 74/5 (746-747).
Refs: 14
ISSN: 0041-1337 CODEN: TRPLAU
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 009 Surgery
026 Immunology, Serology and Transplantation
028 Urology and Nephrology
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English

L101 ANSWER 19 OF 40 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2002331589 EMBASE
TITLE: Cardiovascular disease prevention.
AUTHOR: Keevil J.G.; Stein J.H.; McBride P.E.
CORPORATE SOURCE: Dr. J.G. Keevil, Department of Medicine, Section of Cardiovascular Medicine, Univ. of Wisconsin Medical School, #3248 600 Highland Avenue H6/349, Madison, WI 53792, United States. jgk@medicine.wisc.edu
SOURCE: Primary Care - Clinics in Office Practice, (2002) 29/3 (667-696).
Refs: 63
ISSN: 0095-4543 CODEN: PRCADR
PUBLISHER IDENT.: S 0095-4543(02)00012-X
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 017 Public Health, Social Medicine and Epidemiology
018 Cardiovascular Diseases and Cardiovascular Surgery
036 Health Policy, Economics and Management
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English
AB In this chapter, we have reviewed many of the steps necessary for effective CHD risk reduction. The first step in the office setting is to assess the individual CHD risk. This combines the evaluation of current CHD or a "secondary risk equivalent" with the counting of risk factors and in many cases, the absolute risk calculation. The next steps are to consider each of the major modifiable risk factors (hypertension, dyslipidemia, diabetes mellitus, smoking status) to set goals for each and then work to achieve those goals through lifestyle changes and medication therapy. We reviewed each of these risk factors in detail and then turned to a discussion of emerging risk factors that may help "fine-tune" the risk assessment in some borderline cases. We also discussed additional non-invasive testing that is available to the clinician to help refine the assessment of current burden of disease. Finally, we discuss some of the barriers that exist on both a global and local level to effective treatment of CHD risk factors.

L101 ANSWER 20 OF 40 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2003035465 EMBASE
TITLE: Calcium channel antagonists in the treatment of hypertension.
AUTHOR: Weber M.A.
CORPORATE SOURCE: Dr. M.A. Weber, SUNY Health Science Center, 450 Clarkson Avenue, New York, NY 11203-2098, United States. michaelwebermd@cs.com
SOURCE: American Journal of Cardiovascular Drugs, (2002) 2/6 (415-431).
Refs: 76

ISSN: 1175-3277 CODEN: AJCDDJ
COUNTRY: New Zealand
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 018 Cardiovascular Diseases and Cardiovascular Surgery
030 Pharmacology
036 Health Policy, Economics and Management
037 Drug Literature Index
038 Adverse Reactions Titles
039 Pharmacy
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Calcium channel antagonists are widely used antihypertensive agents. Their popularity among primary care physicians is not only due to their blood pressure-lowering effects, but also because they appear to be effective regardless of the age or ethnic background of the patients. The first available calcium channel antagonists utilized immediate-release formulations which, although effective in patients with angina pectoris, were not approved by the US FDA for use in hypertension. When long-acting once-daily formulations were approved in this indication, the short-acting preparations - which had by then become generic and inexpensive - retained some residual unapproved use for hypertension. An observational case-controlled trial, based on such usage, noted that these agents were associated with a greater risk of myocardial infarctions than conventional agents such as diuretics and .beta.-adrenoceptor antagonists. Further case-controlled trials showed, in fact, that the dangers of calcium channel antagonists were confined to the short-acting agents and that approved long-acting agents were at least as well tolerated and effective as other antihypertensive drugs. Cardiovascular outcomes during treatment with calcium channel antagonists have been examined in randomized, controlled trials. Compared with placebo, the calcium channel antagonists clearly prevented strokes and other cardiovascular events and reduced mortality. The effects of these agents on survival and clinical outcomes were similar to those with other antihypertensive drugs. There is a slight tendency for the calcium channel antagonists to be more effective than other drug types in preventing stroke, but slightly less effective in preventing coronary events. These observations extend to high-risk patients with hypertension including those with diabetes mellitus. Even so, patients with evidence of nephropathy should not receive monotherapy with calcium channel antagonists. Such patients are optimally treated with angiotensin receptor antagonists or ACE inhibitors, although addition of other drugs, including calcium channel antagonists, is often required to achieve the tight blood pressure control necessary to provide adequate renal protection. Calcium channel antagonists have a highly acceptable tolerability profile and careful reviews of available data have shown that their use is not associated with increased bleeding or promotion of tumor formation. It is now recognized that reduction of blood pressure in patients with hypertension to levels often < 130/85mm Hg should be undertaken in presence of other cardiovascular risk factors or evidence of end organ damage. Because of this important concept, calcium channel antagonists, like the other antihypertensive drug classes, are progressively being prescribed less often as monotherapy, but more typically as part of combination regimens.

L101 ANSWER 21 OF 40 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2002301008 EMBASE
TITLE: Intima-media thickness: A new tool for diagnosis and treatment of cardiovascular risk.
AUTHOR: Simon A.; Gariepy J.; Chironi G.; Megnien J.-L.; Levenson J.
CORPORATE SOURCE: Prof. A. Simon, Ctr. de Med. Prev. Cardiovasculaire, Hopital Broussais, 96 Rue Didot, 75674 Paris, France. alain.simon@brs.ap-hop-paris.fr
SOURCE: Journal of Hypertension, (2002) 20/2 (159-169).

Refs: 115
ISSN: 0263-6352 CODEN: JOHYD3
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 017 Public Health, Social Medicine and Epidemiology
018 Cardiovascular Diseases and Cardiovascular Surgery
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Increased intima-media thickness (IMT) is a non-invasive marker of early arterial wall alteration, which is easily assessed in the carotid artery by B-mode ultrasound, and more and more widely used in clinical research. Methods of IMT measurement can be categorized by two approaches: (i) measurement at multiple extracranial carotid sites in near and far walls and (ii) computerized measurement restricted to the far wall of the distal common carotid artery. Because IMT reflects global cardiovascular risk, its normal value might be better defined in terms of increased risk rather than in terms of statistical distribution within a healthy population. The available epidemiological data indicate that increased IMT (at or above 1 mm) represents a risk of myocardial infarction and/or cerebrovascular disease. Close relationships have been shown between: (i) most traditional cardiovascular risk factors; (ii) certain emerging risk factors such as lipoproteins, psychosocial status, plasma viscosity, or hyperhomocysteinemia; and (iii) various cardiovascular or organ damages such as white matter lesion of the brain, left ventricular hypertrophy, microalbuminuria or decreased ankle to brachial systolic pressure index. Thus, IMT gives a comprehensive picture of the alterations caused by multiple risk factors over time on arterial walls. Prospective primary and secondary prevention studies have also shown that increased IMT is a powerful predictor of coronary and cerebrovascular complications (risk ratio from 2 to 6) with a higher predictive value when IMT is measured at multiple extracranial carotid sites than solely in the distal common carotid artery. Therapeutic double-blind trials have shown that lipid-lowering drugs, such as resin and overall statines, and to a lesser extent antihypertensive drugs, such as calcium antagonists, may have a beneficial effect on IMT progression in asymptomatic or in coronary patients. However, methodological standardization of IMT measurement still needs to be implemented before routine measurement of IMT can be proposed in clinical practice as a diagnostic tool for stratifying cardiovascular risk in primary prevention and for aggressive treatment decision. It can be anticipated however, that the presence of increased carotid IMT in one individual with intermediate cardiovascular risk would lead to his classification into the high-risk category and thus influence the aggressiveness of risk factor modifications. .COPYRGT. 2002 Lippincott Williams & Wilkins.

L101 ANSWER 22 OF 40 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2001404067 EMBASE
TITLE: Ongoing clinical trials in systemic hypertension.
AUTHOR: Mann J.; Oddou P.
CORPORATE SOURCE: J. Mann, Speedel Group, Hirschgaesslein 11, 4051 Basel, Switzerland. jessica.mann@speedelgroup.com
SOURCE: Expert Opinion on Investigational Drugs, (2001) 10/11 (2031-2037).
Refs: 39
ISSN: 1354-3784 CODEN: EOIDER
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 006 Internal Medicine
018 Cardiovascular Diseases and Cardiovascular Surgery
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English

SUMMARY LANGUAGE: English
AB Hypertension was identified as a cardiovascular risk factor in the late fifties and still remains a public health issue. The number of patients treated reaches only half of those diagnosed and, of those treated, half fail to reach target blood pressure. Furthermore, the number of antihypertensive drugs reaching the market has increased exponentially in the last few years, however, the impact on treatment and on attaining target blood pressure levels remains to be seen. The high percentage of treated patients who do not reach target blood pressure, combined with the high number of patients requiring more than one antihypertensive drug, have triggered a series of long-term morbidity and mortality trials comparing different therapeutic approaches ('new' pharmacological classes vs. 'old' pharmacological classes). These are described in this paper.

L101 ANSWER 23 OF 40 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2001195446 EMBASE
TITLE: Rationale, design, methods and baseline demography of participants of the Anglo-Scandinavian cardiac outcomes trial.
AUTHOR: Sever P.S.; Dahlof B.; Poulter N.R.; Wedel H.; Beevers G.; Caulfield M.; Collins R.; Kjeldsen S.E.; McInnes G.T.; Mehlsen J.; Nieminen M.; O'Brien E.; Ostergren J.
CORPORATE SOURCE: Prof. P.S. Sever, Clinical Pharmacology, Imperial College School of Medicine, St. Mary's Hospital, London W2 INY, United Kingdom. p.sever@ic.ac.uk
SOURCE: Journal of Hypertension, (2001) 19/6 (1139-1147).
Refs: 36
ISSN: 0263-6352 CODEN: JOHYD3
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 006 Internal Medicine
018 Cardiovascular Diseases and Cardiovascular Surgery
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Objective. To test the primary hypothesis that a newer antihypertensive treatment regimen (calcium channel blocker .+-. an angiotensin converting enzyme inhibitor) is more effective than an older regimen (.beta.-blocker .+-. a diuretic) in the primary prevention of coronary heart disease (CHD). To test a second primary hypothesis that a statin compared with placebo will further protect against CHD endpoints in hypertensive subjects with a total cholesterol .ltoreq. 6.5 mmol/I. Design. Prospective, randomized, open, blinded endpoint trial with a double-blinded 2 x 2 factorial component. Setting. Patients were recruited mainly from general practices. Patients. Men and women aged 40-79 were eligible if their blood pressure was .gtoreq. 160 mmHg systolic or .gtoreq. 100 mmHg diastolic (untreated) or .gtoreq. 140 mmHg systolic or .gtoreq. 90 mmHg diastolic (treated) at randomization. Interventions. Patients received either amlodipine (5/ 10 mg) .+-. perindopril (4/8 mg) or atenolol (50/ 100 mg) .+-. bendroflumethiazide (1.25/2.5 mg) +K(+) with further therapy as required to reach a blood pressure of .ltoreq. 140 mmHg systolic and 90 mmHg diastolic. Patients with a total cholesterol of .ltoreq. 6.5 mmol/I were further randomized to receive either atorvastatin 10 mg or placebo daily. Main outcome measure. Non-fatal myocardial infarction (MI) and fatal coronary heart disease (CHD). Results 19 342 men and women were initially randomized, of these 10 297 were also randomized into the lipid-lowering limb. All patients had three or more additional cardiovascular risk factors. Conclusions. The study has 80% power (at the 5% level) to detect a relative difference of 20% in CHD endpoints between the calcium channel blocker-based regimen and the .beta.-blocker-based regimen. The lipid-lowering limb of the study has 90% power at the 1% level to detect a relative difference of 30% in CHD endpoints between groups. .COPYRGT. 2001 Lippincott Williams & Wilkins.

L101 ANSWER 24 OF 40 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2001339907 EMBASE
TITLE: Effects of atorvastatin (and blood pressure lowering comparing amlodipide-based therapy with beta-blocker-based therapy) on serum variables of cholesterol synthesis and absorption, thrombogenicity and on low-density lipoprotein oxidation in vivo.
AUTHOR: Nieminen M.S.; Viikari J.; Ahotupa M.; Vasankari T.; Kantola I.; Strandberg T.; Vanhanen H.
CORPORATE SOURCE: Prof. M.S. Nieminen, Department of Medicine, Division of Cardiology, Helsinki University Hospital, Haartmaininkatu 4, 00290 Helsinki, Finland
SOURCE: Journal of Human Hypertension, (2001) 15/SUPPL. 1 (S27-S29).
Refs: 21
ISSN: 0950-9240 CODEN: JHHYEN
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 018 Cardiovascular Diseases and Cardiovascular Surgery
029 Clinical Biochemistry
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English

L101 ANSWER 25 OF 40 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2000387438 EMBASE
TITLE: Hypertension drug trials: Past, present, and future.
AUTHOR: Sever P.S.; Poulter N.R.
CORPORATE SOURCE: Prof. N.R. Poulter, Department of Clinical Pharmacology, Imperial College, School of Medicine, London W2 1PG, United Kingdom. n.poulter@ic.ac.uk
SOURCE: Journal of Human Hypertension, (2000) 14/10-11 (729-738).
Refs: 48
ISSN: 0950-9240 CODEN: JHHYEN
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 018 Cardiovascular Diseases and Cardiovascular Surgery
037 Drug Literature Index
017 Public Health, Social Medicine and Epidemiology
038 Adverse Reactions Titles
003 Endocrinology
LANGUAGE: English

L101 ANSWER 26 OF 40 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2000051399 EMBASE
TITLE: Sex bias and underutilization of lipid-lowering therapy in patients with coronary artery disease at academic medical centers in the United States and Canada.
AUTHOR: Miller M.; Byington R.; Hunninghake D.; Pitt B.; Furberg C.D.
CORPORATE SOURCE: Dr. M. Miller, Division of Cardiology, University of Maryland Hospital, 22 S Greene St, Baltimore, MD 21201, United States. mmiller@heart.umaryland.edu
SOURCE: Archives of Internal Medicine, (14 Feb 2000) 160/3 (343-347).
Refs: 18
ISSN: 0003-9926 CODEN: AIMDAP
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 006 Internal Medicine
018 Cardiovascular Diseases and Cardiovascular Surgery
037 Drug Literature Index

LANGUAGE: English
SUMMARY LANGUAGE: English
AB Background: The efficacy of lipid-lowering therapy (LLT) has been well established for patients with preexisting coronary artery disease (CAD). However, limited information is available assessing the extent to which these medications are prescribed in academic medical centers. Methods: The use of LLT for patients with CAD was prospectively evaluated in 825 men and women who were recruited from 16 academic medical centers in the United States and Canada to participate in the Prospective Evaluation of the Vascular Events of Norvasc Trial (PREVENT). The assessment of LLT use during the 3-year trial was evaluated in patients receiving amlodipine therapy and placebo; levels of low-density lipoprotein cholesterol (LDL-C) were used to assess the impact of LLT. Results: Despite a baseline prevalence of LLT in 42% of men (38% in 1994), half of the patients had high levels of LDL-C (>3.36 mmol [>130 mg/dL]). During the subsequent 3 years, the prevalence of elevated LDL-C levels dropped in men (29%) but remained stagnant in women (48%). These changes were associated with increased LLT in men (55%) but not in women (35%) (P = .04). In 1994, the LDL-C target goal (<2.59 mmol/L [<100 mg/dL]) was attained in 17% of men and 6% of women (P = .006). At study completion in 1997, the LDL-C target goal was achieved in 31% of men and only 12% of women (P = .001). Conclusions: This study highlights the relatively low treatment rates of hyperlipidemia among patients with CAD overall and women in particular who were participating in a clinical trial at academic medical centers in the United States and Canada. Because LLT has been proven to reduce future cardiovascular events, these results suggest that more intensive efforts should be promoted in order to maximize CAD reduction.

L101 ANSWER 27 OF 40 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 1999195920 EMBASE
TITLE: [An overview of hypertension studies with calcium antagonists].
OVERSIKT OVER HYPERTENSJONSSTUDIER MED KALSIUMANTAGONISTER.
AUTHOR: Kjeldsen S.E.; Midtbo K.; Os I.; Westheim A.
CORPORATE SOURCE: S.E. Kjeldsen, Hjerte-og Nyremedisinske Avd., Medisinsk Klinikk, Ullevaal Sykehus, 0407 Oslo, Norway
SOURCE: Tidsskrift for den Norske Laegeforening, (20 May 1999) 119/13 (1878-1882).
Refs: 36
ISSN: 0029-2001 CODEN: TNLAAH
COUNTRY: Norway
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 006 Internal Medicine
018 Cardiovascular Diseases and Cardiovascular Surgery
037 Drug Literature Index
LANGUAGE: Norwegian
SUMMARY LANGUAGE: English; Norwegian
AB Calcium antagonists are widely used in the treatment of hypertension. However, few endpoint studies with calcium antagonists have been done to prove reduction in hypertensive complications. Results of the STONE, SYST-EUR and SYST-CHINA studies show that long-acting calcium antagonists are effective compared to placebo, especially in patients with isolated systolic hypertension and diabetes. Ongoing prospective and randomized trials like STOP II, INSIGHT, NORDIL, ALLHAT and ASCOT will clarify whether calcium antagonists are more effective than well-proven diuretics and betablockers. ASCOT will test the hypothesis that amlodipine is more efficacious than atenolol in preventing cardiac complications in 18,000 hypertensive patients with high coronary risk including diabetes (among them, 2,000 in Norway). The study is also randomizing the patients in a factorial design to either atorvastatin or placebo, testing the socalled lipid hypothesis.

L101 ANSWER 28 OF 40 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.

ACCESSION NUMBER: 1999372816 EMBASE
TITLE: Prevention of complications in type 2 diabetes mellitus.
AUTHOR: Wolffenbuttel B.H.R.; Drzewoski J.
CORPORATE SOURCE: Dr. B.H.R. Wolffenbuttel, Dept. of Endocrinology/Metabolism, University Hospital Maastricht, PO Box 5800, NL-6202 AZ Maastricht, Netherlands. bwo@sint.azm.nl
SOURCE: Medical Science Monitor, (1999) 5/5 (1013-1019). Refs: 37 ISSN: 1234-1010 CODEN: MSMOFR
COUNTRY: Poland
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 003 Endocrinology
006 Internal Medicine
018 Cardiovascular Diseases and Cardiovascular Surgery
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English

AB It is expected that the number of patients suffering from diabetes mellitus will increase in the near future. The high rate of microvascular and macrovascular complications developing in these patients will place an even higher burden on our health care systems. Several pathophysiological factors are involved in the development of complications, among which the hyperglycaemia per se, the consequent formation of advanced glycation end products and the intracellular accumulation of sorbitol. In addition, hypertension and dyslipidaemia also play an important role, especially in the development of coronary heart disease and stroke. The major therapeutic goals in type 2 diabetic patients are to optimize blood glucose control, to reduce overweight and to normalize lipid disturbances and elevated blood pressure, in order to improve the well-being of the patient and reduce the risk for the development of late diabetic complications. The UKPDS has clearly demonstrated that achievement of near-normoglycaemia - with sulfonylurea and/or insulin - can reduce the severity of microvascular complications, and that aggressive lowering of elevated blood pressure - with a beta-blocker or an ACE inhibitor - reduces both micro- and macrovascular complications. Secondary intervention studies have demonstrated the beneficial effects of treatment with beta-blockers, aspirin, and inhibitors of cholesterol synthesis, in diabetic patients after myocardial infarction or with angina pectoris. For coronary revascularisation, a preference for CABG in comparison with PTCA in diabetic patients with coronary multivessel disease was suggested. In addition, aggressive near-normalisation of blood glucose levels in the acute phase of myocardial infarction improves prognosis, and reduces 1-year mortality by 31%.

L101 ANSWER 29 OF 40 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 1999057325 EMBASE
TITLE: 71st Annual Scientific Meeting of the American Heart Association, Dallas, Texas, 9-11 November 1998.
AUTHOR: Wroe C.D.
CORPORATE SOURCE: C.D. Wroe, 22b Brunswick Place, Hove BN3 1NA, United Kingdom
SOURCE: International Journal of Clinical Practice, (1999) 53/1 (72-74). Refs: 0 ISSN: 1368-5031 CODEN: IJCPF
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Conference Article
FILE SEGMENT: 006 Internal Medicine
017 Public Health, Social Medicine and Epidemiology
018 Cardiovascular Diseases and Cardiovascular Surgery
037 Drug Literature Index
LANGUAGE: English

L101 ANSWER 30 OF 40 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 1999074562 EMBASE
TITLE: Journal of Cardiovascular Pharmacology: Introduction.
AUTHOR: Sever P.S.; Oparil S.
CORPORATE SOURCE: Dr. P.S. Sever, Imperial College School of Medicine, St. Mary's Hospital, Department of Clinical Pharmacology, London W2 1NY, United Kingdom
SOURCE: Journal of Cardiovascular Pharmacology, (1999) 33/SUPPL. 2 (v-vi).
ISSN: 0160-2446 CODEN: JCPCDT
COUNTRY: United States
DOCUMENT TYPE: Journal; Editorial
FILE SEGMENT: 018 Cardiovascular Diseases and Cardiovascular Surgery
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English

L101 ANSWER 31 OF 40 USPATFULL
ACCESSION NUMBER: 2003:11200 USPATFULL
TITLE: Therapeutic combination
INVENTOR(S): Buch, Jan, Greenwich, CT, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2003008904	A1	20030109
APPLICATION INFO.:	US 2002-214058	A1	20020807 (10)

RELATED APPLN. INFO.: Division of Ser. No. US 2000-512914, filed on 25 Feb 2000, GRANTED, Pat. No. US 6455574 Continuation of Ser. No. WO 1998-IB1225, filed on 11 Aug 1998, UNKNOWN

	NUMBER	DATE
PRIORITY INFORMATION:	US 1997-57275P	19970829 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: Gregg C. Benson, Esquire, Pfizer, Inc., Patent Department, Eastern Point Road, Groton, CT, 06340
NUMBER OF CLAIMS: 117
EXEMPLARY CLAIM: 1
LINE COUNT: 1756
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB This invention relates to pharmaceutical combinations of **amlodipine** or a pharmaceutically acceptable acid addition salt thereof and **atorvastatin** or a pharmaceutically acceptable salt thereof, kits containing such combinations and methods of using such combinations to treat subjects suffering from angina pectoris, atherosclerosis, combined hypertension and hyperlipidemia and to treat subjects presenting with symptoms of cardiac risk, including humans. This invention also relates to additive and **synergistic** combinations of **amlodipine** and **atorvastatin** whereby those **synergistic** combinations are useful in treating subjects suffering from angina pectoris, atherosclerosis, combined hypertension and hyperlipidemia and those subjects presenting with symptoms of cardiac risk, including humans.
IT **88150-42-9, Amlodipine 111470-99-6, Amlodipine** besylate **134523-00-5, Atorvastatin 134523-03-8, Atorvastatin** calcium
(antihypertensive and antihyperlipidemic compns. contg. **amlodipine** and **atorvastatin**)

L101 ANSWER 32 OF 40 USPATFULL
ACCESSION NUMBER: 2002:186125 USPATFULL

TITLE: Combination therapy
INVENTOR(S): Scott, Robert Andrew Donald, Riverside, CT, UNITED STATES
PATENT ASSIGNEE(S): Pfizer Inc. (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2002099046	A1	20020725
APPLICATION INFO.:	US 2001-45329	A1	20011023 (10)

RELATED APPLN. INFO.: Continuation of Ser. No. US 2000-513887, filed on 25 Feb 2000, ABANDONED

	NUMBER	DATE
PRIORITY INFORMATION:	WO 1998-IB1230	19980811
	US 1997-57276P	19970829 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: Gregg C. Benson, Pfizer Inc., Patent Department, Box 519, Eastern Point Road, Groton, CT, 06340
NUMBER OF CLAIMS: 67
EXEMPLARY CLAIM: 1
LINE COUNT: 1775
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB This invention relates to pharmaceutical combinations of **atorvastatin** or a pharmaceutically acceptable salt thereof and antihypertensive agents, kits containing such combinations and methods of using such combinations to treat subjects suffering from angina pectoris, atherosclerosis, combined hypertension and hyperlipidemia and to treat subjects presenting with symptoms of cardiac risk, including humans. This invention also relates to additive and **synergistic** combinations of **atorvastatin** or a pharmaceutically acceptable salt thereof and antihypertensive agents whereby those **synergistic** combinations are useful in treating subjects suffering from angina pectoris, atherosclerosis, combined hypertension and hyperlipidemia and those subjects presenting with symptoms of cardiac risk, including humans.

IT **134523-00-5, Atorvastatin 134523-03-8, Atorvastatin** calcium
(combination therapy comprising **atorvastatin** and antihypertensive agent)

L101 ANSWER 33 OF 40 USPATFULL
ACCESSION NUMBER: 2002:99493 USPATFULL
TITLE: **Synergistic** effect of **amlodipine** and **atorvastatin** on cholesterol crystal formation inhibition and aortic endothelial cell nitric oxide release
INVENTOR(S): Mason, R. Preston, Manchester, MA, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2002052394	A1	20020502
APPLICATION INFO.:	US 2001-921479	A1	20010803 (9)

	NUMBER	DATE
PRIORITY INFORMATION:	US 2000-223214P	20000804 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: PERKINS, SMITH & COHEN LLP, ONE BEACON STREET, 30TH FLOOR, BOSTON, MA, 02108
NUMBER OF CLAIMS: 84

EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 7 Drawing Page(s)
LINE COUNT: 825
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The combination of the antihypertensive calcium channel blocker **amlodipine** and lipid-lowering agent **atorvastatin** inhibits free cholesterol crystallization in atherosclerotic-like membranes. In addition, treatment with a combination of **amlodipine** and **atorvastatin** results in a **synergistic** effect on the release of NO from rabbit aorta endothelial cells.

IT **88150-42-9, Amlodipine 88150-42-9D, Amlodipine**, derivs. **111470-99-6, Amlodipine** besylate **134523-00-5, Atorvastatin 134523-00-5D, Atorvastatin**, hydroxylated metabolites and derivs. **134523-03-8, Atorvastatin** hemicalcium (**amlodipine-atorvastatin synergistic** effect on inhibition of cholesterol crystn. and on NO release in endothelial cells)

L101 ANSWER 34 OF 40 USPATFULL
ACCESSION NUMBER: 2002:43614 USPATFULL
TITLE: Combination therapy
INVENTOR(S): Buch, Jan, Greenwich, CT, UNITED STATES
Scott, Robert Andrew Donald, Riverside, CT, UNITED STATES
PATENT ASSIGNEE(S): Pfizer Inc. (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2002025981	A1	20020228
APPLICATION INFO.:	US 2001-975765	A1	20011010 (9)

RELATED APPLN. INFO.: Continuation of Ser. No. US 2000-513889, filed on 25 Feb 2000, ABANDONED

	NUMBER	DATE
PRIORITY INFORMATION:	WO 1998-IB1220	19980810
	US 1997-57555P	19970829 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: Gregg C. Benson, Pfizer Inc., Patent Department, Box 519, Groton, CT, 06340
NUMBER OF CLAIMS: 106
EXEMPLARY CLAIM: 1
LINE COUNT: 2024
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB This invention relates to pharmaceutical combinations of **amlodipine** or a pharmaceutically acceptable acid addition salt thereof and statins or pharmaceutically acceptable salts thereof, kits containing such combinations and methods of using such combinations to treat subjects suffering from angina pectoris, atherosclerosis, combined hypertension and hyperlipidemia and to treat subjects presenting with symptoms of cardiac risk, including humans. This invention also relates to additive and **synergistic** combinations of **amlodipine** or a pharmaceutically acceptable acid addition salt thereof and statins or pharmaceutically acceptable salts thereof whereby those additive and **synergistic** combinations are useful in treating subjects suffering from angina pectoris, atherosclerosis, combined hypertension and hyperlipidemia and those subjects presenting with symptoms of cardiac risk, including humans.

IT **88150-42-9, Amlodipine 111470-99-6, Amlodipine** besylate

(combination therapy comprising **amlodipine** and HMG-CoA reductase inhibitors)

L101 ANSWER 35 OF 40 USPATFULL
ACCESSION NUMBER: 2002:37338 USPATFULL
TITLE: Drug delivery system for averting pharmacokinetic drug **interaction** and method thereof
INVENTOR(S): Sawada, Toyohiro, Fujieda-shi, JAPAN
Sako, Kazuhiro, Yaizu-shi, JAPAN
Yoshioka, Tatsunobu, Yaizu-shi, JAPAN
Watanable, Shunsuke, Fujieda-shi, JAPAN

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2002022054	A1	20020221
APPLICATION INFO.:	US 2001-834414	A1	20010412 (9)

	NUMBER	DATE
PRIORITY INFORMATION:	US 2000-197574P	20000417 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: TOWNSEND AND TOWNSEND AND CREW, TWO EMBARCADERO CENTER, EIGHTH FLOOR, SAN FRANCISCO, CA, 94111-3834
NUMBER OF CLAIMS: 15
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 1 Drawing Page(s)
LINE COUNT: 1496
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention is a system for averting undesirable pharmacokinetic drug **interaction** between a drug and concomitant drug(s), which consists of controlling the in vivo release time and/or release site of the drug and/or the concomitant drug.
IT **88150-42-9, Amlodipine 134523-00-5, Atorvastatin**
(drug delivery system for avoiding pharmacokinetic **interaction** between drugs and method thereof)

L101 ANSWER 36 OF 40 USPATFULL
ACCESSION NUMBER: 2002:8500 USPATFULL
TITLE: Vasopeptidase Inhibitors to treat isolated systolic hypertension
INVENTOR(S): Reeves, Richard A., Pennington, NJ, UNITED STATES
Wolf, Robert A., Newton, PA, UNITED STATES
Chang, Paul I., Doylestown, PA, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2002004500	A1	20020110
APPLICATION INFO.:	US 2001-819549	A1	20010328 (9)

	NUMBER	DATE
PRIORITY INFORMATION:	US 2000-194499P	20000403 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: MARLA J MATHIAS, BRISTOL-MYERS SQUIBB COMPANY, PATENT DEPARTMENT, P O BOX 4000, PRINCETON, NJ, 08543-4000
NUMBER OF CLAIMS: 13
EXEMPLARY CLAIM: 1
LINE COUNT: 284
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Vasopeptidase inhibitors, especially omapatrilat, are useful in treating

isolated systolic hypertension. The vasopeptidase inhibitor may be used in combination with other pharmaceutically active agents.

IT **111470-99-6, Amlodipine** besylate **134523-03-8, Atorvastatin** calcium
(vasopeptidase inhibitors, alone or with other agents, for treatment of isolated systolic hypertension)

L101 ANSWER 37 OF 40 USPATFULL

ACCESSION NUMBER:	2002:246773 ~~USPATFULL~~
TITLE:	Therapeutic combination
INVENTOR(S):	Buch, Jan, Greenwich, CT, United States
PATENT ASSIGNEE(S):	Pfizer Inc., New York, NY, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6455574	B1	20020924
APPLICATION INFO.:	US 2000-512914		20000225 (9)
RELATED APPLN. INFO.:	Continuation of Ser. No. WO 1998-IB1225, filed on 11 Aug 1998		

	NUMBER	DATE
PRIORITY INFORMATION:	US 1997-57275P	19970829 (60)

DOCUMENT TYPE:	Utility
FILE SEGMENT:	GRANTED
PRIMARY EXAMINER:	Moezie, Minna
ASSISTANT EXAMINER:	Jiang, S.
LEGAL REPRESENTATIVE:	Richardson, Peter C., Benson, Gregg C., Ronau, Robert T.
NUMBER OF CLAIMS:	12
EXEMPLARY CLAIM:	1
NUMBER OF DRAWINGS:	0 Drawing Figure(s); 0 Drawing Page(s)
LINE COUNT:	1428

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB This invention relates to pharmaceutical combinations of **amlodipine** or a pharmaceutically acceptable acid addition salt thereof and **atorvastatin** or a pharmaceutically acceptable salt thereof, kits containing such combinations and methods of using such combinations to treat subjects suffering from angina pectoris, atherosclerosis, combined hypertension and hyperlipidemia and to treat subjects presenting with symptoms of cardiac risk, including humans. This invention also relates to additive and **synergistic** combinations of **amlodipine** and **atorvastatin** whereby those **synergistic** combinations are useful in treating subjects suffering from angina pectoris, atherosclerosis, combined hypertension and hyperlipidemia and those subjects presenting with symptoms of cardiac risk, including humans.

IT **88150-42-9, Amlodipine 111470-99-6, Amlodipine** besylate **134523-00-5, Atorvastatin 134523-03-8, Atorvastatin** calcium
(antihypertensive and antihyperlipidemic compns. contg. **amlodipine** and **atorvastatin**)

L101 ANSWER 38 OF 40 USPATFULL

ACCESSION NUMBER:	2001:214406 USPATFULL
TITLE:	Method of analyzing data ~~from a circulating blood~~ viscometer for determining absolute and effective blood viscosity
INVENTOR(S):	Kensey, Kenneth, Chester Springs, PA, United States Hogenauer, William N., Gilbertsville, PA, United States Cho, Young, Cherry Hill, NJ, United States
PATENT ASSIGNEE(S):	Visco Technologies, Inc., Exton, PA, United States

(U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6322525	B1	20011127
APPLICATION INFO.:	US 2000-501856		20000210 (9)

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 1999-439795, filed on 12 Nov 1999 Continuation-in-part of Ser. No. US 1997-919906, filed on 28 Aug 1997, now patented, Pat. No. US 6019735

DOCUMENT TYPE: Utility
FILE SEGMENT: GRANTED
PRIMARY EXAMINER: Winakur, Eric F.
ASSISTANT EXAMINER: Wingood, Pamela
LEGAL REPRESENTATIVE: Casar, Rivise, Bernstein, Cohen & Pokotilow, Ltd.
NUMBER OF CLAIMS: 84
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 11 Drawing Figure(s); 9 Drawing Page(s)
LINE COUNT: 1468
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A method is provided for detecting **interactions** in the circulating blood of a living being caused by external factors by analyzing the viscosity of the living being's circulating blood. The method utilizes a blood viscosity measuring system that monitors the change in height of two, oppositely-moving, columns of blood from the circulating blood of a patient and, given the dimensions of a capillary tube through which the blood flows, determines the blood viscosity over a range of shear rates, especially low shear rates. The system includes a tube set that includes a pair of riser tubes, a capillary tube of predetermined dimensions that is coupled between the riser tubes and a valve mechanism for controlling the circulating flow of blood from the patient into the riser tubes. Respective sensors monitor the movement of the columns of blood in each of the riser tubes and an associated microprocessor analyzes these movements, along with the predetermined dimensions of the capillary tube to determine the viscosity of the patient's circulating blood. A first viscosity profile is determined over a first shear rate range and a second viscosity profile is determined over the first shear rate range and a second shear rate range. The method utilizes the relationship of these two viscosity profiles, as well as with respect to a horizontal line, to detect the **interactions** in the circulating blood of a living being caused by the external factors. Furthermore, the tube set can then be pivoted clockwise and/or counterclockwise for measuring platelet aggregation and red blood cell deformability. In addition, a method and apparatus for determining the yield stress of the blood is discussed, as well as a method for determining the effects of drugs designed to treat a condition of the living being.

IT **88150-42-9, Amlodipine 134523-00-5, Atorvastatin**
(app. and methods for monitoring blood viscosity and other parameters in drug delivery for diagnostics and treatment)

L101 ANSWER 39 OF 40 WPIDS (C) 2003 THOMSON DERWENT
ACCESSION NUMBER: 1999-214611 [18] WPIDS
DOC. NO. CPI: C1999-063222
TITLE: Use of a **synergistic** combination of **amlodipine** and a statin compound for treating angina pectoris and atherosclerosis.
DERWENT CLASS: B03
INVENTOR(S): BUCH, J; SCOTT, R A D
PATENT ASSIGNEE(S): (PFIZ) PFIZER PROD INC; (PFIZ) PFIZER INC
COUNTRY COUNT: 84
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9911263	A1	19990311	(199918)*	EN	55
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG ZW					
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE GH GM HR HU ID IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZW					
AU 9884585	A	19990322	(199931)		
ZA 9807843	A	20000426	(200027)		55
NO 2000000999	A	20000228	(200029)		
EP 1003507	A1	20000531	(200031)	EN	
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MK NL PT RO SE SI					
CZ 2000000319	A3	20000816	(200048)		
BR 9811558	A	20000822	(200050)		
SK 2000000139	A3	20000814	(200051)		
CN 1268054	A	20000927	(200067)		
HU 2000003103	A2	20010131	(200118)		
MX 2000002085	A1	20001001	(200158)		
KR 2001022385	A	20010315	(200159)		
JP 2001514224	W	20010911	(200167)		61
US 2002025981	A1	20020228	(200220)		
AU 744982	B	20020307	(200229)		
NZ 502283	A	20020531	(200246)		

APPLICATION DETAILS:

PATENT NO	KIND		APPLICATION	DATE
WO 9911263	A1		WO 1998-IB1220	19980810
AU 9884585	A		AU 1998-84585	19980810
ZA 9807843	A		ZA 1998-7843	19980828
NO 2000000999	A		WO 1998-IB1220	19980810
			NO 2000-999	20000228
EP 1003507	A1		EP 1998-935246	19980810
			WO 1998-IB1220	19980810
CZ 2000000319	A3		WO 1998-IB1220	19980810
			CZ 2000-319	19980810
BR 9811558	A		BR 1998-11558	19980810
			WO 1998-IB1220	19980810
SK 2000000139	A3		WO 1998-IB1220	19980810
			SK 2000-139	19980810
CN 1268054	A		CN 1998-808465	19980810
HU 2000003103	A2		WO 1998-IB1220	19980810
			HU 2000-3103	19980810
MX 2000002085	A1		MX 2000-2085	20000228
KR 2001022385	A		KR 2000-700964	20000128
JP 2001514224	W		WO 1998-IB1220	19980810
			JP 2000-508366	19980810
US 2002025981	A1	Provisional	US 1997-57555P	19970829
		Cont of	US 2000-513889	20000225
			US 2001-975765	20011010
AU 744982	B		AU 1998-84585	19980810
NZ 502283	A		NZ 1998-502283	19980810
			WO 1998-IB1220	19980810

FILING DETAILS:

PATENT NO	KIND	PATENT NO

AU 9884585	A	Based on	WO 9911263
EP 1003507	A1	Based on	WO 9911263
CZ 2000000319	A3	Based on	WO 9911263
BR 9811558	A	Based on	WO 9911263
HU 2000003103	A2	Based on	WO 9911263
JP 2001514224	W	Based on	WO 9911263
AU 744982	B	Previous Publ.	AU 9884585
		Based on	WO 9911263
NZ 502283	A	Based on	WO 9911263

PRIORITY APPLN. INFO: US 1997-57555P 19970829

AB WO 9911263 A UPAB: 20011203

NOVELTY - Use of a **synergistic** combination of **amlodipin** (I) and a statin (II) compound produces a **synergistic** antihypertensive, hypolipidemic, antianginal or antiatherosclerotic effect.

DETAILED DESCRIPTION - A composition comprises:
(a) (I) (disclosed in US 4,572,909) or a salt;
(b) (II) (not **atorvastatin**) or a salt; and
(c) a carrier or diluent.

INDEPENDENT CLAIMS are included for the following:
(i) separate compositions of (I) and (II) for use together
(ii) a kit comprising (a), (b), (c) in a container.

ACTIVITY - Antihypertensive; hypolipidemic; antianginal; antiatherosclerotic.

MECHANISM OF ACTION - Calcium channel blocker (I); HMG-CoA reductase inhibitor (II).

USE - The combination is useful for treating angina pectoris, atherosclerosis, combined hypertension and hyperlipidemia, and subjects with symptoms of cardiac risk.

ADVANTAGE - The combination of (a) and (b) is **synergistic**. No suitable data given.

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L101 ANSWER 40 OF 40 WPIDS (C) 2003 THOMSON DERWENT

ACCESSION NUMBER:	1999-204972 [17] WPIDS
DOC. NO. CPI:	C1999-059655
TITLE:	Use of a **synergistic** combination of **atorvastatin** and antihypertensive agent for treating angina pectoris and atherosclerosis.
DERWENT CLASS:	B03 B05
INVENTOR(S):	SCOTT, R A D
PATENT ASSIGNEE(S):	(PFIZ) PFIZER INC
COUNTRY COUNT:	84

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9911260	A1	19990311	(199917)*	EN	51
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG ZW					
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE GH GM HR HU ID IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZW					
AU 9884589	A	19990322	(199931)		
ZA 9807839	A	20000426	(200027)		49
NO 2000000996	A	20000427	(200032)		
EP 1009400	A1	20000621	(200033)	EN	
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MK NL PT RO SE SI					
CZ 2000000342	A3	20000816	(200048)		
BR 9811556	A	20000822	(200050)		

CN 1268053 A 20000927 (200067)
SK 2000000143 A3 20001211 (200103)
HU 2000004318 A2 20010528 (200140)
KR 2001022477 A 20010315 (200159)
JP 2001514223 W 20010911 (200167)
AU 740424 B 20011101 (200175)
AU 2002014783 A 20020321 (200230)#
MX 2000002086 A1 20010801 (200238)
US 2002099046 A1 20020725 (200254)
NZ 502280 A 20021122 (200301)

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APPLICATION DETAILS:

PATENT NO	KIND		APPLICATION	DATE
WO 9911260	A1		WO 1998-IB1230	19980811
AU 9884589	A		AU 1998-84589	19980811
ZA 9807839	A		ZA 1998-7839	19980828
NO 2000000996	A		WO 1998-IB1230	19980811
			NO 2000-996	20000228
EP 1009400	A1		EP 1998-935250	19980811
			WO 1998-IB1230	19980811
CZ 2000000342	A3		WO 1998-IB1230	19980811
			CZ 2000-342	19980811
BR 9811556	A		BR 1998-11556	19980811
			WO 1998-IB1230	19980811
CN 1268053	A		CN 1998-808463	19980811
SK 2000000143	A3		WO 1998-IB1230	19980811
			SK 2000-143	19980811
HU 2000004318	A2		WO 1998-IB1230	19980811
			HU 2000-4318	19980811
KR 2001022477	A		KR 2000-701062	20000131
JP 2001514223	W		WO 1998-IB1230	19980811
			JP 2000-508363	19980811
AU 740424	B		AU 1998-84589	19980811
AU 2002014783	A	Div ex	AU 1998-84589	19980811
			AU 2002-14783	20020201
MX 2000002086	A1		MX 2000-2086	20000228
US 2002099046	A1	Provisional	US 1997-57276P	19970829
		Cont of	US 2000-513887	20000225
			US 2001-45329	20011023
NZ 502280	A		NZ 1998-502280	19980811
			WO 1998-IB1230	19980811

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 9884589	A	Based on	WO 9911260
EP 1009400	A1	Based on	WO 9911260
CZ 2000000342	A3	Based on	WO 9911260
BR 9811556	A	Based on	WO 9911260
HU 2000004318	A2	Based on	WO 9911260
JP 2001514223	W	Based on	WO 9911260
AU 740424	B	Previous Publ.	AU 9884589
		Based on	WO 9911260
AU 2002014783	A	Div ex	AU 740424
NZ 502280	A	Div in	NZ 520177
		Based on	WO 9911260

PRIORITY APPLN. INFO: US 1997-57276P 19970829; AU 2002-14783 20020201
AB WO 9911260 A UPAB: 20011203

NOVELTY - Use of a combination of **atorvastatin** and an antihypertensive agent produces a **synergistic** antihypertensive, hypolipidemic, antianginal or antiatherosclerotic effect.

DETAILED DESCRIPTION - A composition comprises:

(a) **atorvastatin** (disclosed in US4681893) or a salt;

(b) an antihypertensive agent (not **amlodipine**) or a salt; and

(c) a carrier or diluent.

INDEPENDENT CLAIMS are included for separate compositions of (a) and (b) for use together, and kits containing combinations of (a) and (b).

ACTIVITY - Antihypertensive; hypolipidemic; antianginal; antiatherosclerotic.

MECHANISM OF ACTION - None given.

USE - The combination is useful for treating angina pectoris, atherosclerosis, combined hypertension and hyperlipidemia, and subjects with symptoms of cardiac risk.

ADVANTAGE - The combination of (a) and (b) is **synergistic**.

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FILE 'HOME' ENTERED AT 12:01:04 ON 26 FEB 2003